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The Clinical Trial 113
A. Bradford Hill

Acute Perforated Peptic Ulcer. 119
Stanley Mikal and William R. Morrison

Chronic Idiopathic Hypertrophic Osteoarthropathy 123
Morris Berk

Medical Progress: Hospital Administration. . 127
Nathaniel W. Faxon

Medical Intelligence:
A New Self-Retaining Electrocardiographic Electrode 131
Eugene Lepeschkin

Rubella in Pregnancy 132

Case Records of the Massachusetts General Hospital 133

Editorials:
Clinical Accountancy 142
Roentgenographic Studies of the Intervertebral Disk. 143
Home-Town People. 144

Massachusetts Medical Society 144
Massachusetts Department of Public Health . 144
Correspondence 145
Nonclinical Notes 146
Books Received 147
Notices 148

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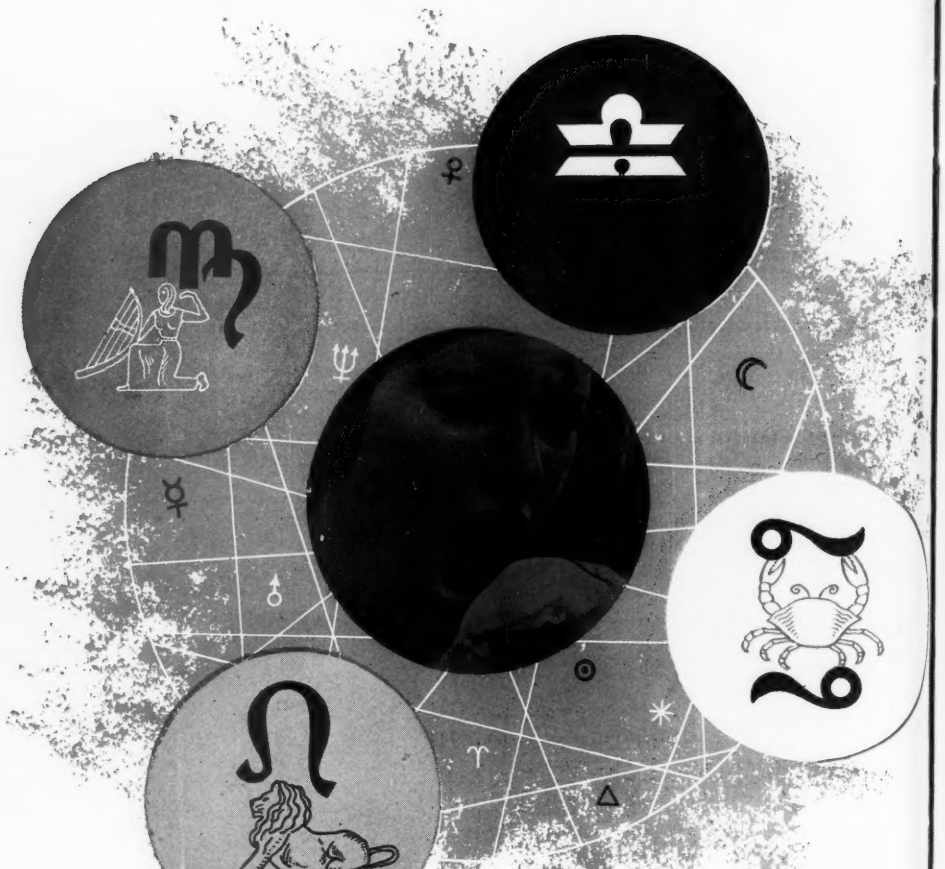

In hay fever

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THE CLINICAL TRIAL*

A. Bradford Hill, C.B.E., D.Sc., Ph.D.†

LONDON, ENGLAND

IT IS with mixed feelings that I stand, a layman, before the medical faculty of one of the world's most famous universities. In the past century, or more, statisticians have, it is true, been recognized as having a right of entry to the field of public health, and to its related sciences of epidemiology and preventive medicine. They have been closely associated with medical officers of health. They have worked with all who have been concerned with the promotion and maintenance of the well-being of the community. But it is clear that the health of the community — the group — essentially requires the statistical approach. For we are concerned with the herd rather than with the individual and so we need community measures. I might hope to speak on matters of mutual interest to your School of Public Health. I might, of course, prove boring to it, but I should speak as a bore, not as a stranger. I should promote sleep rather than catcalls; that belief gives me courage. What, however, of your University's Medical School? Dare the statistician now pass from the well tilled (perhaps I ought to say well drained) fields of public health to those more exclusive upland meadows in which are practiced the arts of the clinician — arts that appear to cultivate the individual approach and sometimes even an air of infallibility? It is a bold step. In my own country I have been fortunate enough to be able to take it and can, even at the worst, still exclaim, with the poet Henley, "my head is bloody but unbowed." Over a fairly wide expanse of clinical medicine in Great Britain the statistical approach has been accepted as useful; it is being increasingly applied. But here, like Ruth "amid the alien corn," I stand, if not tearfully, at least a trifle fearfully.

Before setting out I sought support in an anonymous article on Statistics in Medicine that formed part of the *British Medical Journal's* instructive review of the progress of British medicine in the first half of the present century. Between statistician and clinician there had been, it confesses, antagonism: "The medical man charged with responsibility for the patient was contemptuous of the statistician's fundamental approach through the group; and the statistician took a jaundiced view of the conclusions light-heartedly drawn by the practitioner from a handful of cases without allowance for the play of chance."[1] The only comforting thing about that statement is its use — an apparently deliberate use — of the past tense. Has, then, the antagonism gone? I believe it is undoubtedly very much less than it used to be. But I could not lay my hand upon my heart and say it has vanished wholly. There are still noticeable from time to time, in medical journals and at meetings of medical societies, various kinds and degrees of mutual misunderstanding and even scorn. Before launching out upon the philosophy of a clinical trial, I think it would be well to consider them.

Misunderstandings and Mistakes

The Statistician

Let me first place in the dock those of my own profession. The statistician, and particularly those not in close contact with clinical medicine, may tend to forget that the physician's first duty is to his patient — to do all in his power to save the patient's life and restore him, as rapidly as possible, to health. That fundamental and ethical duty must never be overlooked — though with the introduction of better, brighter and ever more toxic drugs, and with the wide prevalence of surgical procedures such as tonsillectomy, the onlooker may perhaps with good reason sometimes ask the clinician "are you sure you know where that duty lies?" It seems to me sometimes to be unethical *not* to experiment, not to carry out a controlled clinical trial. But we must never forget the issues. Basically, too, the statistician is concerned with things that can be counted. "In so far as things, persons, are unique or ill-defined, statistics are meaningless . . . ; in so far as things are similar and definite . . . they can be counted and new statistical facts are born . . . Our arithmetic is useless unless we are counting the right things."[2] Clearly, until that happy day ar-

*Read before the Department of Preventive Medicine, Harvard Medical School, May 28, 1952 and based partly on a discussion held at the Medical Society of London, November, 1951.

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rives when every clinician is his own statistician, we need a close collaboration to ensure that the statistician *is* counting the right things — for instance, that he is devising satisfactory groups into which patients can be classified, and that he is setting up the most appropriate and definite measures of the patient's condition before and after treatment. I have seen friction arise through the statistician's inability to do this through a lack of knowledge of the medical problem and of its details.

The art of applied statistics is, needless to say, compounded of two things — a knowledge of statistical methodology and a wide and detailed knowledge of the data to which that methodology is to be applied. I should hesitate to allocate a relative importance to each of these two aspects, but I hold firmly that both are essential and that the use of the methodology, however erudite, without a parallel and exact knowledge of the data under study can be, indeed is likely to be, most dangerous. It follows that the statistician, if he is to play his proper part in a clinical trial must be in it "up to his neck"; he must be in it from its very start — that is, at the initial planning level. If he is a layman he must endeavor to learn and understand its medical as well as its statistical aspects — and should, I believe, be as intensely absorbed and interested in the one as in the other. As a corollary he should almost invariably decline to be brought in at the end of a trial merely to sort out and add up the results or, even worse, to calculate as a kind of super bookmaker, the odds for or against some event of whose pros and cons he is largely ignorant and about which he could not care less. Too often, he makes the mistake of accepting such a task. In short, the statistically designed clinical trial is above all a work of collaboration between clinician and statistician, and that collaboration must prevail from start to finish.

Finally, in my indictment of the statistician, I would argue that he may tend to be a trifle too scornful of the clinical judgment, the clinical impression. Such judgments are, I believe, in essence, statistical. The clinician is attempting to make a comparison between the situation that faces him at the moment and a mentally recorded but otherwise untabulated past experience. There clearly may be gain in the introduction of more objective and more quantitative methods of assessment, which can be recorded, than can be supplied by this clinical instinct. Certainly no harm will be done, as Sir Henry Dale[3] has pointed out, if these newer and more objective methods of observation "are used primarily to supplement, and only by careful stages and with proved advantage to replace, the older and subjective ones. The loss, if any, would arise from haste to discard a coherent though impressionistic picture, and to replace it by a collection of precise but as yet uncoordinated details." At present I would argue that we should, whenever possible, endeavor to harness the clinical impression to our measurements of the results of a therapeutic trial. To that I shall return again.

The Clinician

Turning now to the other side of the picture — the attitude of the clinician — I would, from experience, say that the most frequent and the most foolish criticism of the statistical approach in medicine is that human beings are too variable to allow of the contrasts inherent in a controlled trial of a remedy. In other words, each patient *is* "unique" and so there can be nothing for the statistician to count. But if this is true it has always seemed to me that the bottom falls out of the clinical approach as well as the statistical. If each patient is unique, how can a basis for treatment be found in the past observations of other patients? In fact, of course, physicians do not act like that. They base their "method of choice" upon what they have seen happen before — whether it be in only two or three cases or in a score. But even if human beings are not each unique in their responses to a given treatment they are certainly likely to be variable, sometimes extremely variable. Two or three uncontrolled observations may, therefore, give merely through the customary play of chance, a favorable picture in the hands of one doctor, an unfavorable picture in the hands of a second. And so the medical journals, euphemistically called the "literature," are cluttered up with conflicting claims — each in itself perfectly true of what the doctor saw, and each insufficient to bear the weight of the generalization placed upon it.

Far, therefore, from arguing that the statistical approach is impossible in the face of human variability, we should realize that it is because of that variability that it is often essential. It does not follow, to meet another common criticism of the statistical approach, that it invariably demands large numbers. It may do so; it depends upon the problem. But, it should be recognized, the responses to treatment of a single patient are clearly a statement of fact — so far as the observations were truly made and accurately recorded. And that single case may give, in certain circumstances, evidence of vital importance.

If, for example, we were to use a new drug in a proved case of acute leukemia and the patient made an immediate and indisputable recovery, should we not have a result of the most profound importance? The reason underlying our acceptance of merely one patient as illustrating a remarkable event — not necessarily of cause and effect — is that long and wide experience has shown that in their response to acute leukemia human beings are *not* variable. They one and all fail to make immediate and indisputable recoveries. They one and all die. Therefore, although it would clearly be most unwise upon this one case to pass from the particular to the general, it would be sheer madness

not to accept the evidence presented by it. No statistician (no statistician, let me say, who knew his subject matter) would object to that sample on the grounds that it was too small to be informative.

If, on the other hand, the drug were given to a patient suffering from acute rheumatic fever and the patient made an immediate and indisputable recovery, the statistician might suggest (with customary diffidence) that we have little basis for remark. That recovery may clearly have followed the administration of the drug without the slightest probability of a related cause and effect. With this disease human beings *are* variable in their reactions, — some may die, some may have prolonged illnesses but recover eventually with or without permanent damage, some may make immediate and indisputable recoveries, — whatever treatment we may give them. We must, therefore, have more cases before we can reasonably draw inferences about cause and effect.

I have somewhat labored this point of numbers of observations because the old and fallacious gibe still lingers on, even among persons who should know better: that statisticians would, if given the opportunity, have rejected — or even suppressed, though I am never quite sure how — some of the original and fundamental observations in medicine, on the grounds of their small number. For example, fragilitas ossium, I was once told, was originally described in just two cases; and this number I was also informed, a trifle tartly, "statisticians would regard as useless evidence." Why on earth should they? My retort ran as follows[4]:

> If 'exact descriptions' were given of these two cases and 'beautiful water colours' were supplied to illustrate them, then of course they are scientific evidence, and undeniable evidence of an occurrence — whether it be of one case or two. It would only be in relation to any subsequent appeal from the particular to the general that the statistician — and equally any trained scientific worker — could object. If on the basis of these two cases the clinician (in practice, let us say, near Smithfield Market) should be so unwise as to argue that the condition was specific to butchers, then the statistician might suggest that the experience was both too select and too slender in size to justify any such generalization.

In short there is, and can be, no magic number for either clinician or statistician. Whether we need one, a hundred or a thousand cases turns upon the setting of our problem and the inferences that we wish to draw. Faced with the rapid recovery of a single patient with rheumatic fever under a new drug what, I suggest, the careful clinician would do is not to generalize but to test the treatment on a second case. If it worked well again — or, perhaps, if it did not — he would test it on a third. And, without being accused of undue caution, or even of mathematical leanings, he might go so far as to seek a fourth. Thus, with somewhat halting steps, he unwittingly directs himself up the statistical garden path. I believe he might sometimes fare better if he straightaway walked boldly up the path and without any ado opened the gate to a designed and controlled clinical trial.

The Controlled Trial

The essence of such a trial is comparison. To the dictum of Helmholtz that "all science is measurement," we should add, Sir Henry Dale[3] has pointed out, a further clause that "all true measurement is essentially comparative." Usually, therefore, but again not always, we need not only the group of patients to be submitted to a special treatment, or treatments, under investigation but another group differently treated — by, usually, the older and, at the time, more orthodox methods. The first step in the statistical technic, then, is the *random* allocation of patients to one or other of these groups. (I am, of course, assuming that the ethical situation has first been most carefully considered and the decision reached that such a trial is both proper and possible; if it is not it may yet be possible to devise some other, though probably less informative, type of trial, but with that I am not here concerned.)

There are various ways in which the random allocation of the patients to the treatment groups can be carried out. Most often today and, I think, preferably, it is done by the construction of an order of allocation, unknown in advance to the clinician, and based upon random sampling numbers — a modern substitute for tossing up, and one that is a trifle less embarrassing in the ward or office. Thus using OT to stand for orthodox treatment and NT for new treatment (without necessarily any confession of faith therein) we may have as the order for patients consecutively brought into the trial OT, NT, NT, OT, OT, OT, NT, and so forth. We may easily introduce a device to equalize the number of patients on the new and old treatments at, for example, every dozen — since otherwise by the play of chance we may occasionally be embarrassed by too many of one kind and too few of another. I do not think it necessary to spend time now upon these minutiae. What I would emphasize are the advantages of this random and unpremeditated distribution of patients to groups. Strictly adhered to — and I need hardly say that this is a *sine qua non* — this method ensures three things: it ensures that neither our personal idiosyncrasies (our likes or dislikes consciously or unwittingly applied) nor our lack of balanced judgment has entered into the construction of the different treatment groups — the allocation has been outside our control and the groups are therefore unbiased; it removes the danger, inherent in an allocation based upon personal judgment, that believing we may be biased in our judgments we endeavor to allow for that bias, to exclude it, and that in so doing we may overcompensate and by thus "leaning over backward" introduce a lack of balance from the other direction; and, having used a random allocation, the sternest critic is unable to say when we eventually dash

into print that quite probably the groups were differentially biased through our predilections or through our stupidity. Once it has been decided that a patient is of the right type to be brought into the trial the random method of allocation removes all responsibility from the clinical observer.

It may sometimes, however, be argued — and with truth — that this random allocation gives too much freedom to the play of chance and thus fails to provide groups that are sufficiently alike, or as alike as they could have been if we had used a more deliberate method of distribution. The likelihood of such a failure is clearly dependent upon two things: the size of the groups that we set up and the variability of the patients we bring into them. Often one can effectively meet the difficulty by first dividing the somewhat heterogeneous group of patients who are to be brought into the trial into more homogeneous sub-groups, and then making the random allocation to treatment O, treatment N and so forth within each of the sub-groups. This has been the technic adopted in the joint trials of cortisone and ACTH versus salicylates in rheumatic fever now being carried out to a common plan in a number of centers in the United Kingdom, the United States and Canada. Thus we have six subgroups. Rheumatic fever runs, on the average, a different course in young children and in adolescents. We have, therefore, a subdivision by age into patients under sixteen years old and patients aged sixteen years or over. Apart from age, however, the course of the disease in relation to treatment, particularly with regard to any permanent damage that may occur to the heart, may well be influenced by the speed with which, after the onset of an attack, treatment can be instituted. We have, therefore, within each of the two age groups, three divisions by the duration of time that had elapsed between the recorded onset of attack and the start of treatment: treatment begun within the first two weeks of the illness; treatment begun between two and six weeks after onset; and treatment not begun until more than six weeks had elapsed. Every patient must first satisfy certain criteria of diagnosis, which have been laid down. Being thus eligible for entry to the trial, he is first allocated to whichever of the six subgroups he belongs. He is then allocated to a specific treatment, whether with cortisone, ACTH or salicylates, by means of random orders set up for each of the six subgroups and, separately, for each center taking part in the trial.

It may be, and indeed it is highly likely, that we shall not have enough cases in each of these six more homogeneous subgroups to allow firm conclusions to be drawn. But we shall at least be in the position to amalgamate the six subgroups, if it is justifiable, knowing that the three treatment groups in total will then have the same distribution of patients by age and by duration of illness. By the design of the trial we have ensured equality in the treatment groups in these respects, and by a random allocation applied to the subgroups we have ensured an absence of personal bias.

Such designs, simple though they may be, are of importance. They may often require smaller numbers of patients for the solution of a problem and allow a wider range of questions to be simultaneously tackled. I would usually, however, myself sooner seek a decisive answer to one or two questions than cast my bread upon the waters and be faced finally with seven "not statistically significant" differences. "Not statistically significant," one should always remember, is the equivalent of the "non-proven" of the Scots law rather than the "not guilty" of the English courts. I also emphasize that in spite of the random construction of the treatment groups that I have envisaged, it will in practice be essential to prove that the groups of patients under each treatment have, in fact, turned out to be similar in their features at entry — that is, in such features as may be relevant to a patient's response to treatment. For example, an analysis of the patients at entry to the trial must reveal the level of their temperatures and their blood sedimentation rates, the frequency of their heart murmurs and their bacteriologic companions, and so on. No method of random allocation can absolutely ensure the equality of the groups in all these respects. The goddess of chance may prevent it, particularly when we are concerned with small groups. It is therefore our first and imperative job to show that the groups we have set up are reasonably alike or, if not, to make such allowances as are possible for the differences that have occurred. Such allowances after the event are not always easy to make, and therefore the "stratifying" by subgroups that I have touched upon has considerable advantage in ensuring equalities in major characteristics.

The Treatment

In the great majority of the controlled clinical trials with which I have been associated a specific treatment schedule has been laid down. It may, needless to say, be varied with age or body weight or some other characteristic of the patient; but apart from that it has been rigidly defined in advance and must be adhered to by the clinician (except for the usual over-riding ethical reasons). Clearly, however, in regard to treatment there are an infinite number of questions we can ask of a trial. We can choose one dose out of many; we can vary the interval of administration; we can give it by different routes; we can exhibit it for different lengths of time; and so on. In testing a new form of treatment knowledge at first is necessarily scanty, being usually based upon laboratory work and a few scattered clinical observations. In Medical Research Council trials we have thought it proper, therefore, to choose such a regimen as promised to reveal the potentialities (and often the dangers)

of the drug (or whatever may be concerned). Thus we have a tidy question — for example, if to a defined type of patient 2 gr. of drug X are given daily in four divided doses by intramuscular injection and for three months, what happens?

But perhaps the question is too tidy. We can, of course, extend it after its answer has been reached by experimenting with variations upon the original theme. It may, however, be argued, and sometimes, I think, legitimately, that allowance should have been made during the basic trial for individual idiosyncrasies, that the clinician should have been free to vary the dosage according to his own judgment of the patient's needs as shown by the latter's responses. Statistically, I see no reason why that should not be done so long as two things are observed and remembered. The first is that we have deliberately changed the question asked of the trial; it now runs "if competent clinicians in charge of defined types of patients use drug X in such varying amounts and for such varying durations of time, and so forth, as they think advisable for each patient, what happens?" The moot point is which question, in given circumstances, is the better one to ask. The second point is that at the conclusion of such a trial we can *in no circumstances* compare the effects of the different regimens of treatment that have been used. These regimens have been determined by the conditions and responses of the individual patients; to observe then, at the end of the trial, the patients' differential conditions and responses in relation to their treatments is merely circular reasoning. We cannot possibly measure thus the advantages and disadvantages of differing regimens but only, by an expansion of the controlled trial, include groups randomly allocated to such treatments. The main danger of this free-for-all trial is the apparently almost overpowering attraction to some clinicians of circular motion.

The Answers

These are the opening gambits of the clinical trial — the definition of the patients, their random allocations to the treatment groups, the laying down of the treatment schedule. At the end of play we shall have to add up the score. Clearly the more objective we can make our means of so doing, the safer we shall be from criticism. Naturally, therefore, we turn first to measurable characteristics. Stone-dead has no fellow, and pre-eminent, therefore, stands the number of patients who die. No statistician, so far as I know, has in this respect accused the physician of an over-reliance upon the clinical impression. Fortunately, however (except statistically speaking), many diseases upon which we must test new treatments are not particularly lethal. Other objective characteristics must be sought and are usually found in such features as the duration of fever, the level of the blood sedimentation rate and the presence of infecting organisms. The appropriate measures vary from one disease to another, and I shall not dwell on them now. I would, however, stress that it is essential to decide *before* the trial begins exactly what measurements will be taken, how they will be taken and precisely when. Without those prior decisions chaos will reign. Working under them we shall have measurements by means of which we can see whether the different treatment groups show differences in their average levels of, for example, body temperature or body weight on specified days — and in their ratios, such as the proportion of patients who become afebrile after a given duration of treatment and the proportion who have a raised blood sedimentation rate. Even with prior thought, it is not always a quite simple task to lay down requirements. In another field, that of the law, Lord MacMillan notes that a statute of the reign of King George III enacted that the penalties under the Act were to be given one half to the informer and one half to the poor of the parish. Neither the informer nor the poor would, however, he points out, be likely to be grateful for this benefaction since the only penalty prescribed was fourteen years' transportation to the colonies. If lawyers, with their care for words, can so err, how much more the doctor!

Returning to our answers from the clinical trial, they present, it will be noted, a *group* reaction. They show that one group fared better than another, that given a certain treatment patients, *on the average*, get better more frequently or more rapidly, or both. We cannot necessarily, perhaps very rarely, pass from that to stating exactly what effect the treatment will have on a particular patient. But there is, surely, no way and no method of deciding that. Also it is well to remember that observation of the group does not inhibit the most scrupulous and careful observation of the individual at the same time — if it is believed that more can be learnt that way.

"Whereas I Was Blind, Now I See"

Passing now from such measurable to the less measurable characteristics of disease processes we shall have, in some cases, x-ray evidence and in all of them the clinical assessment to which I referred above. The difficulties inherent in making unbiased and reliable assessments of x-ray films we have endeavored to meet in some Medical Research Council trials, and I think with much success, by having the films read and the radiologic changes assessed by one or more persons, who have in so doing been kept in ignorance of the treatment groups to which the patients belonged. That process resolves to a large extent the problem of bias, and it does not subject the clinician in charge of the case to hardship. The clinical assessment of the patient's progress and of the severity of the illness he has suffered presents considerably greater difficulties. If it is to be used effectively, without fear

and without reproach, the judgments must be made without any possibility of bias, without any overcompensation for a possible bias, and without any possibility of accusation of bias. In other words, the assessment must, whenever possible, be "blind"—the assessing clinician must not know the treatment of the patient. And that, of course, is a difficult procedure to carry out — indeed it is sometimes quite impossible. Thus, in the Medical Research Council's trials of streptomycin in young adult patients with phthisis, in the early days of that antibiotic, the group on streptomycin had to undergo repeated injections — at least twice a day for several months. It would have been out of the question, for very obvious reasons, to give the contrasting group similar injections of an inert substance. There could be no way of disguising the treatment from the clinical observer (in fact, in that particular situation it was not very necessary to do so, for we could judge on the mortality and the radiologic changes that were assessed "blind").

On the other hand, in the Medical Research Council's trial of an antihistaminic drug in the "cure" of the common cold, feelings of enthusiasm or skepticism may well run high in the bosom (or should I say nasal mucosa?) either of the recipient of the drug or of his clinical observer, or indeed of both. If either were allowed to know the treatment that had been given, I believe that few of us would without qualms accept the result that the drug was of value — if such an answer came out of the trial. Here a group given a placebo was essential; here complete ignorance in both patient and doctor of the treatment actually given was essential. It was not very difficult to incorporate both features in the trial (and in passing it is interesting to note that the placebo produced not only the same number of "cures" as the drug but almost as many "side-effects").

Sometimes another possible approach is by means of the administration of a known treatment, such as an injection, by one person and the clinical assessment of the results by another kept in ignorance of that treatment. In short, given a problem of sufficient importance and given sufficient faith in the method, some means of making a "blind" clinical assessment can frequently, if not usually, be devised. It is thus, I suggest, that we may effectively give the "coherent though impressionistic picture" its rightful place in the therapeutic trial.

Responsibilities

Without demanding this "blind approach," or even accurate measurement, it is certainly likely that the mental contrasting of one treatment with another or of a new treatment against the old will give, at least in the hands of able observers, a truthful, if not precise, answer *if* a treatment has a real and considerable effect. Without a strictly controlled trial the merits of a penicillin could not (and, in fact, did not) fail to come to light. With "winners" it is very easy for the critics of the statistical approach to be wise after the event and to say that the general evidence available at the start of a long, and perhaps tedious, trial made it unnecessary or pedantic. They tend — conveniently to themselves — to forget the occasions when the trial has shown that a treatment has little, if any, value — in spite of the general "evidence" that was available. The history of medicine is, surely, sullied by the reigns of such vulgar upstarts whose prestige, lacking a scientific test, lingered on, to the detriment of human welfare.

It is easy to point out to critics, too, that it is difficult to determine through clinical impressions whether a drug is quite useless or of some slight but undoubted value, and that it is even more difficult to determine with uncontrolled and unco-ordinated observations whether, today, one powerful antibiotic is more valuable than another in particular situations. For instance, I do not think the relative values of aureomycin, chloramphenicol and penicillin in the treatment of clinical pneumonias could have been clearly determined without a fairly large-scale and carefully controlled trial.[5] In particular, it is frequently important that negative results be proved and proved without undue delay.

These particular criticisms are not difficult to meet. The real difficulty to my mind lies, or may lie, in the charge that a trial is unethical. For instance in a letter to the *British Medical Journal*[6] a writer protesting — in part, I think, justifiably — against present ways of writing scientific papers referred to "the replacement of humanistic and clinical values by mathematical formulae," the degradation of patients "from human beings to bricks in a column, dots in a field, or tadpoles in a pool" and "the eventual elimination of the responsibility of the doctor to get the individual back to health." This appears to me to be in essence an attack upon the clinical trial, though the writer at the same time admitted that "since science is mensuration, a sound statistical survey of any particular form of treatment is of importance." I am impressed by the editorial comment in the same issue of the *British Medical Journal*, a comment that expresses what I feel and could not myself, I am sure, have put more clearly:

> It is difficult to see how the results of this 'sound statistical survey' can be analyzed other than by a 'sound statistical method' and presented otherwise than in a 'sound statistical table,' with, if necessary, mathematical formulae. By so doing, in what way are we degrading the patients and shirking our responsibility as doctors to get the individual back to health? The whole essence of the survey is to see whether a new treatment will benefit patients. There appear to be two ways of going to work. We may try it on John Smith and Mary Robinson and report the results — that John Smith got well quickly and Mary Robinson, poor soul, died. We have done our best for both. Or we may try it on 30 John Smiths and 20 Mary Robinsons and report the numbers that lived and died. It is likely that the larger numbers will be found more informative than the smaller. But have we done

any less for the 50 than we did for the two? Further, if there be no ethical reasons to forbid — a paramount and overriding proviso — we may contrast the 30 John Smiths and 20 Mary Robinsons with an equal number of men and women not given this new and wholly unproved drug. Wherein have we shirked our duties? In treating patients with unproved remedies we are, whether we like it or not, experimenting on human beings, and a good experiment well reported may be more ethical and entail less shirking of duty than a poor one.

As R. A. McCance,[7] professor of experimental medicine at Cambridge University, has pointed out, "the medical profession has a responsibility not only for the cure of the sick and for the prevention of disease but for the advancement of knowledge upon which both depend. This third responsibility can be met only by investigation and experiment." The statistically guided therapeutic trial is not the only means of investigation and experiment, nor indeed is it invariably the best way of advancing knowledge of therapeutics. I commend it to you as *one* way, and, I believe, a useful way, of discharging that third responsibility to mankind.

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ACUTE PERFORATED PEPTIC ULCER*

Criteria for Operation and Analysis of 500 Cases

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THE purpose of this paper is to present an analysis of 500 consecutive cases of acutely perforated peptic ulcers admitted to the Boston City Hospital from January, 1938, to May, 1950, and to attempt to present some criteria for selecting the perforations that should be treated surgically and those that should be treated nonsurgically.

There were 471 males and 29 females, a ratio of 16:1. Four hundred and seventy-one patients were white, 25 were Negro and 4 were oriental. Most were between the ages of thirty and sixty, but 75 cases occurred after the age of sixty (Fig. 1). The youngest patient was a girl fourteen years of age; the oldest, a woman of eighty-four. A slight increase in the number of perforations occurred in the fall, as compared to other seasons. Perforation occurred in 90 patients while they were at work, 351 during rest and 59 during sleep. The acute catastrophe of perforation appeared to be the first sign of an ulcer in 84 cases. The remaining 406 patients had had ulcer symptoms for from a few weeks to five years. Operation for perforated peptic ulcer had previously been performed in 8.6 per cent of the cases.

Three cardinal symptoms and signs of perforation were: sudden onset of acute abdominal pain, restlessness and abdominal rigidity. The pain often simulated, in order of frequency, that of acute cholecystitis, acute pancreatitis, coronary occlusion, appendicitis, diaphragmatic pleurisy and small-bowel obstruction. Although the abdominal wall was usually tense and spastic, abdominal distention was present in 8 per cent (40 cases). Hematemesis and melena occurred in 12.8 per cent (64 cases) and was associated with multiple peptic ulcers in 15 cases. Any patient with a perforated peptic ulcer associated with bleeding should be suspected of having multiple ulcers.

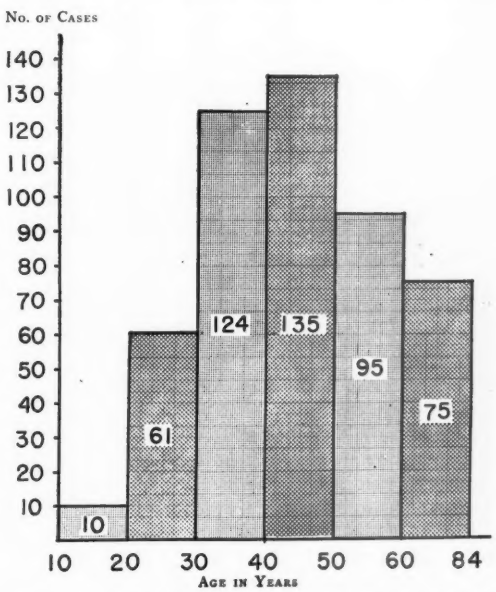

Figure 1. *Age Distribution of Patients with Perforated Peptic Ulcers.*

Three hundred and twelve patients had x-ray films for pneumoperitoneum, and in 232, or 74.4 per

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cent, air was visualized under the diaphragm. The incidence of pneumoperitoneum was noted to increase as the duration of perforation increased (Fig. 2). During the first three hours of perforation, only 30 per cent showed positive evidence of pneumoperitoneum. In the succeeding third to sixth hours of perforation, 66 per cent had pneumoperitoneum. After the seventh hour of perforation, the incidence of pneumoperitoneum was almost 100 per cent. If the technic of DeBakey had been used, — inserting a Levine tube and blowing

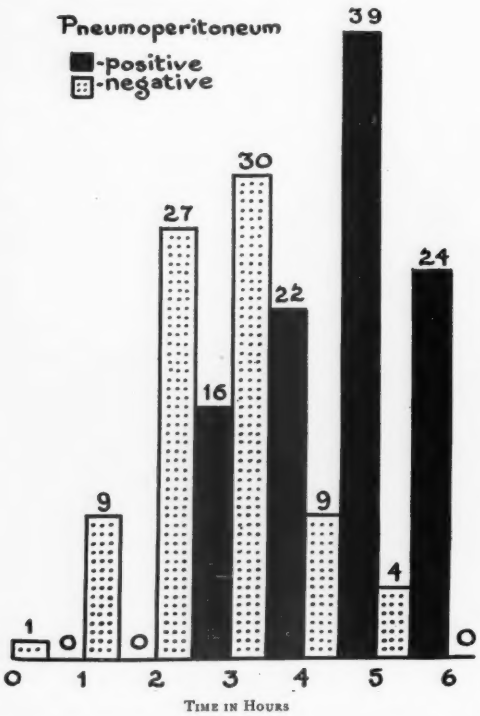

FIGURE 2. *Relation of Pneumoperitoneum to Duration of Perforation.*

30 cc. of air into the stomach, — the incidence of pneumoperitoneum would have been much greater in the first six hours of perforation. Moreover, if all patients were made to sit up for ten minutes prior to x-ray examination, the incidence of pneumoperitoneum would have been much higher. However, these last two procedures were infrequently performed in this series of cases. Subcutaneous emphysema is seldom associated with perforated peptic ulcers but was noted in 5 cases. Shock was an inconspicuous feature of perforated peptic ulcers, being present preoperatively in only 25 cases. Urinary diastases were performed in 70 cases; 12.6 per cent showed values of over 300 Somogyi units. Differentiating acute pancreatitis and perforated peptic ulcer proved difficult on occasions, especially in the absence of pneumoperitoneum.

Pathology

Two hundred and twenty-seven perforations were located in the duodenum, 203 in the stomach, 13 at the pylorus and 7 at the gastrojejunal stoma. Sometimes edema, exudate or fibrin distorted anatomic landmarks such as the pyloric sphincter, pyloric vein of Mayo or supraduodenal artery of Wilkie, making it difficult to determine the exact site of perforation. In 37 cases the surgeon reported that the perforation was prepyloric, but subsequent x-ray examination revealed that a healed ulcer or deformity of the duodenum could be demonstrated, and there was no evidence of a gastric ulcer. Of the perforated gastric ulcers, 4 were in the cardia, 4 in the posterior wall and 2 along the greater curvature. It is interesting to note that these gastric ulcers were all benign. In one case, multiple peptic ulcers of the duodenum perforated simultaneously. Roberts[1] reported a similar case; Bell and others[2] reported a case of two perforations in a single duodenal ulcer. Stobie[3] reported the simultaneous perforation of a duodenal and a gastric ulcer. Peptic ulcers often perforate into adjacent structures and organs such as the gall bladder,[4] pancreas,[5] liver,[6] spleen,[5] diaphragm,[7] lung,[7] bile ducts,[8] gastrohepatic ligament,[5] and anterior abdominal wall.[9] Levine[10] reported a case in which a perforated duodenal ulcer caused complete obstruction of the common bile duct.

The average size of the perforations was 5 mm. in diameter; they ranged from 2 to 30 mm. in diameter. A positive culture of the peritoneal fluid was obtained in 126 cases. The organisms cultured, in order of frequency, were streptococcus, staphylococcus, colon bacillus, *Clostridium perfringens* (*B. welchii*), diphtheroids, Monilia, enterococci, *Proteus vulgaris*, *Aerobacter aerogenes*, *Alkaligenes faecalis*, pneumococci and *B. pyocyaneus* (*Pseudomonas aeruginosa*).

Treatment

Four hundred and sixty-eight perforations were treated surgically, 32 medically. Simple closure was performed in 452 cases. Eleven cases were submitted to primary subtotal gastrectomy and 5 had simple closure of the perforation with complementary gastroenterostomy. An omental graft was employed in 271 cases. Spinal anesthesia was used in 408 cases; local or inhalation anesthesia was resorted to in 60 poor-risk patients. For routine closure of a perforated ulcer, we prefer a one- or two-layered closure, using either fine silk or catgut for a seromuscular Lembert stitch with the suture line lying in the long axis of the stomach or duodenum (Fig. 3).

The total operative mortality for this series of cases was 13.8 per cent (68 cases), the total non-

operative mortality 84.3 per cent (27 cases). The nonoperative mortality was high because the patients selected for this form of treatment were usually moribund or in shock.

Three hundred and seventy-nine operative cases received antibiotics or sulfonamides intravenously, intraperitoneally or orally, either singly or in combination, with a mortality rate of 8.7 per cent (33 cases). Prior to the era of sulfonamides and antibiotics, the operative mortality was 36 per cent (32 deaths in 89 operative cases). For the years 1948, 1949 and 1950, the operative mortality for simple closure of perforated ulcers dropped to 4.2 per cent. This increase in the survival rate may be attributed to such factors as antibiotics, early operation, advances in parenteral nutrition, early ambulation and better training of surgical residents.

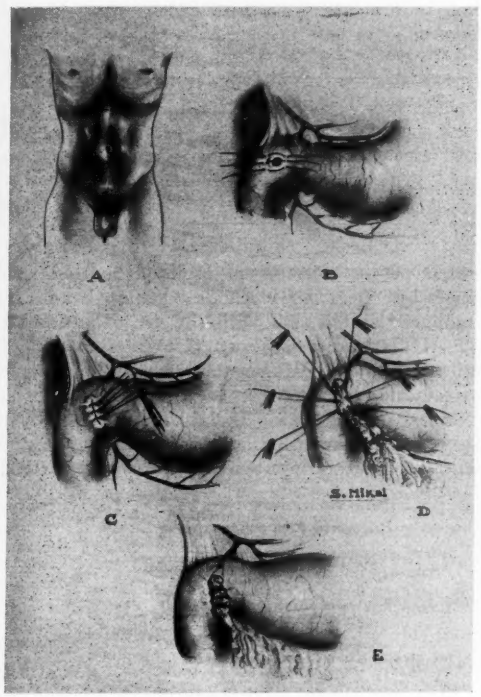

FIGURE 3. *Technic of Closure of a Perforated Peptic Ulcer.* A = *Types of abdominal incisions that may be used — right rectus-splitting incision, subcostal muscle-retracting or muscle-cutting incision and transverse muscle-retracting or muscle-cutting incision.* B = *Lembert seromuscular sutures placed across the ulcer.* C = *Sutures tied and ulcer inverted.* D = *A pedicled graft of omentum laid between the long ends of the sutures.* E = *Sutures tied over the omental graft.*

It is our opinion that sex and location of the ulcer affect the prognosis very little. However, age and the time lapse after perforation are dominant factors in the prognosis. Mortality rates rise significantly when the perforations are over twelve hours old and the patients are over fifty years of age (Fig. 4 and 5). Three hundred and seventy-nine patients had antibiotic therapy. Of these, 124 were operated on within the first six hours of perforation,

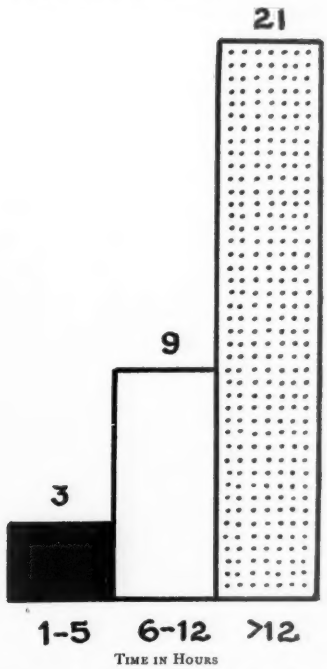

FIGURE 4. *Operative Mortality in Patients Receiving Antibiotics or Sulfonamides Contrasted with Duration of Perforation.*

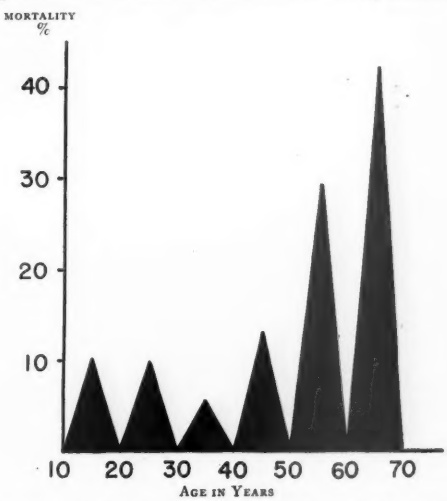

FIGURE 5. *Relation of Mortality in Perforated Peptic Ulcer to Age of Patient.*

with a mortality of 2.5 per cent (3 cases); 174 were operated on six to twelve hours after perforation,

with a mortality of 5.2 per cent (9 cases); and 81 cases were operated on with perforations over twelve hours old, with a mortality of 25.9 per cent (21 cases). Of the patients who died, 8 had multiple ulcers, and 3 had massive hemorrhage with postoperative exsanguination. In 7 cases, the perforations, which were supposed to have been surgically closed, continued to leak postoperatively. Four patients died of pulmonary embolism. The postoperative complications included 73 dehiscences, 6 eviscerations, 5 gastric or duodenal fistulas, 18 subphrenic abscesses and 13 pelvic abscesses. The commonest complications were pulmonary — atelectasis, pneumonia, emphysema and pulmonary edema. Although it is not the purpose of this paper to describe the follow-up studies of these patients, it is interesting to note that 59 later had subtotal gastrectomies, 2 had posterior gastroenterostomies, 23 developed recurrent ulcers that were not operated on and 3 died of reperforation. Williams[11] reviewed the follow-up status of patients with perforated ulcers at the Boston City Hospital and reported that 23 per cent had poor results, 22 per cent had fair results and the remainder had good results.

TABLE 1. *Operative Deaths Following Subtotal Gastrectomy for Perforated Peptic Ulcer.*

YEAR	INVESTIGATOR	NO. OF CASES	DEATHS	COMPLICATIONS
1940	DeBakey[9]	2392	321	Not compiled
1944	Graves[12]	20	1	Not compiled
1944	Strauss[13]	8 (selected)	0	1 postoperative pneumonia
1945	Bisgard[14]	5 (selected)	0	1 subphrenic abscess (recovered) 1 pneumonia with wound disruption (recovered)
1948	Bobbio[15]	29	0	2 duodenal fistulas (recovered)
1950	Timpone and Gross[22]	16	0	0

TABLE 2. *Mortality for Conservative Treatment of Perforated Peptic Ulcers.*

YEAR	INVESTIGATOR	NO. OF CASES	DEATHS	COMPLICATIONS
1945	Bedford-Turner[17]	6 (unstated)	0	0
1946	Taylor[18]	24 (consecutive)	3	1 generalized peritonitis (died) 1 pulmonary embolus (died)
1946	Visick[19]	13 (consecutive)	3	1 pneumonia (died) 1 subphrenic abscess (recovered) 1 subphrenic abscess (died)
1947	Birks[23]	9 (selected)	0	0
1948	Bingham[20]	5 (selected)	0	0
1949	Seeley (et al.)[21]	34 (consecutive)	0	2 subphrenic abscess (recovered) 1 pleural effusion (recovered)
1950	Bertram[24]	16 (consecutive)	0	1 subphrenic abscess (recovered)

DISCUSSION

There is much controversy concerning whether perforated ulcers should be treated operatively or nonoperatively. There is also much debate about which operative procedure should be employed, simple closure or subtotal gastrectomy. The preferred method of treatment in most hospitals is simple closure of the ulcer. The reason for its popularity is that it is simple and can be performed by any surgeon. A more radical approach to the problem is immediate subtotal gastrectomy, as advocated by Graves,[12] Strauss,[13] Bisgard,[14] Bobbio[15] and Yudine.[16] The nonoperative management of acutely perforated peptic ulcers has recently been popularized by Bedford-Turner,[17] Taylor,[18] Visick,[19] Bingham[20] and Seeley.[21] The fundamentals in the conservative treatment of perforated peptic ulcers are: nothing by mouth; gastric suction; morphine; antibiotics; and intravenously administered fluids. The results of the nonoperative treatment of perforated peptic ulcers seem as good as those obtained by operative methods (Tables 1 and 2). Zinninger[25] stated that with the use of antibiotics and ACTH or adrenal cortical extracts combined with sedation and Wangensteen suction, many more patients may be treated in the future by nonoperative means. The reason that so much controversy exists concerning whether conservative management or operative intervention is the best method of treatment is that the criteria for selecting the proper procedure have not been clearly defined.

We propose that simple operative closure be performed for the following conditions: perforations exhibiting early signs of spreading peritonitis; perforations already associated with generalized peritonitis; formes-frustes ulcers that exacerbate with a focal peritonitis; perforations over twenty-four hours old that continue to leak (even in poor-risk patients); conditions in which the diagnosis is uncertain and the patient fails to improve under conservative treatment; and perforations with multiple ulcers or cases with a previous history of perforation in which the age or condition of the patient warrants a minimal procedure.

Primary subtotal gastrectomy may be selected under optimal operative conditions for patients who are in good health, are under fifty years of age, are not in shock, and have perforations of less than

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twelve hours' duration. Therefore it may be employed for patients with: questionable carcinoma with perforation; pyloric obstruction associated with perforated ulcer; perforations with multiple ulcers; multiple perforations; perforations with hemorrhage; or a history of previous perforation.

Conservative management may be instituted for: formes-frustes ulcers; ulcers less than twelve hours old that show signs of improvement; perforations attended by shock; late perforations that have sealed off or formed an abscess; and cases in which the diagnosis is equivocal.

With regard to the follow-up of patients with perforated peptic ulcer, we follow Wangensteen's[26] advice to recommend subtotal gastrectomy six weeks to two months after recovery from the perforation. This view has recently been re-emphasized by Luer[27] and Turner.[28]

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CHRONIC IDIOPATHIC HYPERTROPHIC OSTEOARTHROPATHY*

Report of a Case and Review of the Literature

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THE clinician is often confronted with clubbed fingers in an otherwise healthy person. However, idiopathic hypertrophic osteoarthropathy, or clubbing with extensive bone and joint changes without underlying etiologic disease, is a rarity. Only recently has this subject been clarified,[1] the literature having been confused by a variety of titles such as "familial acromegaloid osteosis," "idiopathic familial generalized osteophytosis," "hypertrophic pulmonary osteoarthropathy without primary disease" and "acropachydermia with pachyperiostitis." As mentioned by Camp and Scanlan,[1] these terms have been used because of certain characteristics of the disease, such as its familial tendency, its superficial resemblance to acromegaly and its similarity to other forms of osteoarthropathy, and because of skin and skeletal changes. These authors were able to find only three references to this condition in the American literature.[2-4] Five of their own cases bring the record total in this country to 8, whereas 21 cases have been found reported in foreign periodicals. Because of this small number, it seemed worth while to report another such case. It is my purpose to stress the importance of differentiating idiopathic and secondary osteoarthropathy, because of the high incidence of pulmonary cancer associated with the latter.

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Case Report

A 25-year-old Negro laborer, was admitted to the Veterans Hospital on March 22, 1949, complaining of pain with swelling in the lower legs and ankles. These symptoms began gradually in the fall of 1945, continuing without remission until his hospital admission. The pain was worse on prolonged weight bearing and in the morning, when it was associated with stiffness. In the course of time he noted bony enlargement of the ankles. Clubbing of the fingers was first called to his attention early in 1946 at another hospital. A chest roentgenogram was normal at that time. No definite change in the degree of clubbing was observed since its discovery.

The patient's history disclosed a 40- to 50-lb. weight gain in 1942 that began shortly after his induction into the Armed Forces. This took place over several months, without associated symptoms.

System review revealed frequent upper-respiratory infections during the preceding 2 years. Between these episodes he had no cough or sputum and no hemoptysis, fever, chills or pain. He had no history of rheumatic fever, syphilis or tuberculosis and no disturbance of libido or potency.

The patient's mother and sister were interviewed and showed no clubbing of the fingers or toes. The mother believed that her son's fingers had been normal in childhood, as were those of 4 other siblings and the patient's father.

Physical examination disclosed a robust, slightly obese, phlegmatic man whose outstanding physical finding was marked clubbing of the fingers (Fig. 1). His weight was

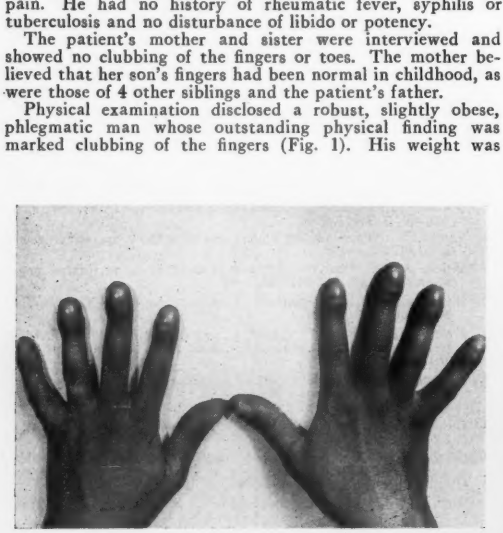

FIGURE 1. *Marked Clubbing of Fingers in Patient with Chronic Idiopathic Hypertrophic Osteoarthropathy.*

186 lb. and his height 70 inches. There were suggestive mongoloid features (epicanthus, short nose, prominent cheekbones). The mandible was small. Striae were seen along the lateral abdominal wall. There were no other skin changes. Breasts, testes, prostate and hair distribution were normal. Bony enlargement with tenderness to firm palpation was noted over the distal third of both legs and the ankle regions. Heart and lungs were normal. Abdominal examination was negative. The blood pressure was 110/70, the pulse 66.

Chest roentgenograms and fluoroscopy showed the heart and lungs to be normal. Bronchograms visualized an entirely normal bronchial tree. Bone survey revealed extensive periosteal changes and cortical thickening involving the lower tibia and fibula bilaterally (Fig. 2 and 3). Similar but less extensive findings were seen in the radius, ulna and femur bilaterally. There was increased tufting of the distal phalanges of both hands. Skull, vertebral column and pelvis were normal. Subsequent roentgenograms over a 3-year period showed a slight increase in periosteal thickening in the involved bones. Barium-enema examination and gastrointestinal roentgenograms were normal. An electrocardiogram was normal.

Examination of the blood revealed a red-cell count of 5,500,000, with a hemoglobin of 15.9 gm. and a white-cell count of 7500 with a normal differential. Examination of the red blood corpuscles for sickling was negative. The urine, sedimentation rate, serum alkaline, serum acid phosphatase and spinal fluid were normal. A blood Kahn test was negative. The blood cholesterol was 200 mg. and the serum protein 6.8 gm. per 100 cc., with 4.48 gm. of albumin and 2.32 gm. of globulin. Culture of a 72-hour sputum concentrate was negative for acid-fast organisms. Skin tests with first- and second-strength tuberculin (PPD) were negative. Basal-metabolism determinations were −5, +1, −13 and −16 per cent. The bromsulfalein retention was 2.5 mg. per 100 cc. in 45 minutes. A cephalin-flocculation test was negative in 24 and 48 hours.

The patient has now been thoroughly studied and periodically followed for nearly 3 years. During this time his symptoms and findings have remained essentially as before except for a slight increase in the periosteal changes. He has continued his work, with little loss of time. All causes of secondary hypertrophic osteoarthropathy have been ruled out. Because of some features suggestive of hypothyroidism and his low basal-metabolism determinations, thyroid was administered for a lengthy period, with neither subjective nor objective change.

DISCUSSION

Chronic idiopathic hypertrophic osteoarthropathy has been described as "a condition occurring predominantly in males at the age of puberty or adolescence and characterized by the osteoarthropathic syndrome; i.e. clubbing of the digits, enlargement of the bones and joints, and thickening of the skin of the face; in the absence of any demonstrable primary disease."[1] Its history dates back to 1890 as part of the group of diseases designated by Marie[5] as "hypertrophic pulmonary osteo-arthropathy," a

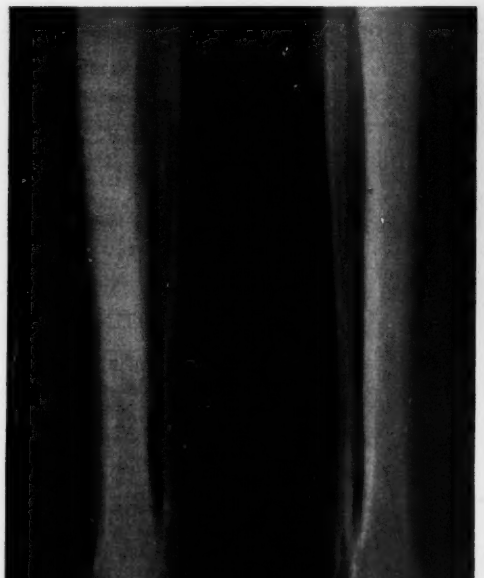

FIGURE 2. *Extreme Periosteal Proliferation of Both Tibias and Fibulas, with "Layering" of Periosteal New Bone Along the Diaphysis.*

syndrome seen in association with a wide variety of primary afflictions. Eventually cases began to appear without evident primary disease. After considerable controversy, culminated by Oehme's studies,[6] it became recognized as an entity with a definite relation to puberty. For this reason Oehme

concluded that it was a constitutional disease caused by endocrine imbalance at that period of life. Nearly all cases so far reported have had their onset in adolescent youths. Fried[7] and Bloom[8] recently furthered the trend of thought along these lines by their post-mortem findings of hyperplasia of eosinophilic cells of the pituitary gland in several cases of secondary osteoarthropathy. There were clinical features suggesting an endocrine disturbance, such as tufting of the terminal phalanges, acromegalic appearance, gynecomastia, hirsutism, mongoloid features and female distribution of hair. Fried, therefore, has suggested that the lungs are endowed with secretory as well as respiratory functions, as originally postulated by Aschoff, Roger,

FIGURE 3. *Irregular Periosteal Proliferation Involving Metaphysis of Tibia and Fibula.*

and others,[9-11] and that in pulmonary disease endocrine disturbances leading to osteoarthropathy are mediated through the pituitary gland. Hereditary predisposition is another possible etiologic factor in the idiopathic cases, as evidenced by the alleged familial involvement in 60 per cent of such cases.[1]

The symptoms of this syndrome are said to follow a predictable pattern, with an insidious onset and a slowly progressive course, often terminating in a standstill. Pathologic changes may be most marked in the bones, joints or skin. The greatest disability occurs in the bones. Bony enlargement is due to lateral growth and usually causes few symptoms other than deformity and low-grade pain. Systemic manifestations are minimal. Roentgenologic features are characteristic and consist chiefly in a slowly progressive ossifying periostitis, beginning in the distal end of the diaphysis and later involving the entire shaft. These changes have been described in nearly all bones but are most often seen in the long bones, ordinarily at the distal thirds of the legs and the forearms. Proliferation is greatest over the diaphysis, is decreased in the region of the metaphysis and is slight over the epiphysis. The ungual tufts are said, as a rule, to undergo atrophy, but normal variations are common. The endosteum is not involved in the hypertrophy, the medullary cavity thus remaining normal. Joint involvement is late in development and is most often seen adjacent to the involved bones.

In regard to the differential diagnosis of this condition, the difficulty lies in distinguishing it not from

FIGURE 4. *Periosteal Proliferation of Lesser Degree, Chiefly Involving the Radius (Metaphysis).*

other bone diseases but from secondary osteoarthropathy, since roentgenographically they are essentially the same, as pointed out by Camp and Scanlan.[1] Secondary osteoarthropathy can be excluded only by considering the history, familial involvement, age at onset, tempo and duration and by ruling out primary disease. These authors mention that other diseases that can cause confusion are acromegaly, rheumatoid arthritis, periostitis (specific and nonspecific), osteitis deformans and osteopetrosis. Secondary osteoarthropathy is definitely the most important disorder to rule out — since it may indicate some serious underlying disease. Especially is this true in relation to cancer of the lung, in which the initial symptoms are often those of the osteoarthropathic syndrome. Patti-

son,[12] for instance, recently reported 5 cases of bronchogenic carcinoma in which the symptoms of hypertrophic osteoarthropathy were the initial ones. Craig[13] also found 4 such cases, with the presenting diagnosis of rheumatoid arthritis in 3 and that of acromegaly in 1. Bone symptoms preceded pulmonary symptoms by from eight to eleven months in all these patients. Another example occurred in a Cabot Case[14] with clubbing and bone symptoms antedating the pulmonary symptoms by one and a half years. The osteoarthropathic syndrome is said to have an acute onset in these cases, to be rapid in tempo and to last for months rather than years, as in the idiopathic type.

Mendolowitz,[15] in referring to secondary osteoarthropathy, mentions that "it may be the barometer of the underlying disease," waxing and waning with the activity of the etiologic lesion. He mentions that complete disappearance of clubbing and occasional bony changes have been described after spontaneous improvement or surgical treatment of the causative condition. Complete disappearance is never noted in hereditary or idiopathic clubbing. Worthy of mention also, as indicated by Mendolowitz, is the formerly held concept that clubbing of the digits and hypertrophic osteoarthropathy were independent phenomena. It is now generally recognized that osteoarthropathic changes have the same causes as clubbing and merely represent a more advanced stage of the process. Osteoarthropathy, for this reason, is considerably less common than simple clubbing but is probably much more common than is indicated by the literature.

Summary and Conclusions

The rare syndrome of idiopathic hypertrophic osteoarthropathy is reviewed and a case is added to the literature. Its onset in puberty and the presence of ungual tufting, abdominal striae and mongoloid facies suggest a probable endocrine etiology.

It is important to differentiate this condition from secondary hypertrophic osteoarthropathy, which not infrequently antedates an underlying neoplasm of the lung.

It is likely that the occurrence of simple clubbed fingers without obvious underlying etiology represents idiopathic osteoarthropathy of milder degree. Roentgenograms in these cases may disclose asymptomatic bone or joint changes.

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MEDICAL PROGRESS

HOSPITAL ADMINISTRATION

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BOSTON

MACEACHERN[1] has said that "The science and art of hospital administration are growing more complex due to the rapidly extending field of hospital service and the advance of scientific medicine."

Hospital administration, which began as a lowly stewardship, is now recognized as an occupational specialty, requiring executive ability and, among other items, a thorough knowledge of public health, social service, business principles, hotel operation, finances, personnel practices and public relations. It is dignified by the conferring of the collegiate degree in hospital administration and under proper qualifications by membership or fellowship in the American College of Hospital Administrators. From a position that was filled by any deserving person in need of a job, regardless of experience or qualifications, it has developed into one that trustees recognize as requiring both ability and training.

From a medical point of view, hospital administration can be classified as an important medical specialty, such as ophthalmology, urology, psychiatry or orthopedics. It may not call for an equal amount of technical skill or scientific knowledge, but it requires a greater understanding of business principles and methods, of economics, of social problems, of finance, of personnel relations and of many other factors. It requires personality, common sense, hard work and a sympathetic understanding of people.

In New England, the change from an unprofessional superintendency by untrained persons to the present exacting requirements of hospital director or administrator began with and was advanced by the wise direction and example of Dr. Herbert H. Howard. Of course, it was not he alone who brought about this change, but as resident physician of the Massachusetts General Hospital and later as superintendent of the Peter Bent Brigham Hospital he greatly influenced the administration of New England hospitals. He was a forceful man with a clear vision of the growing importance of hospitals in medicine and public health. Under his wise guidance many of the present accepted policies of hospital administration were formulated, and many men who were to play an important part in the spreading of these policies were trained.

In 1800 there were only 7 hospitals in the United States. By 1850 there were 87. During the next fifty years 1382 were added; thereafter the number of hospitals increased on an average of over 100 a year, until by 1950 there were over 6500 hospitals in the country.

During the last one hundred years everything in this country was expanding in about the same ratio as hospitals. Although population increased proportionately, there was intense competition for manpower. The tremendous increase in hospitals placed a terrific strain on the resources of the community, which had to supply the trained personnel necessary to operate this growing enterprise. Expanding medical schools supplied the doctors — of varying quality. Hospitals started nursing schools and trained nurses to meet, to some extent, their growing needs. Superintendents or administrators were drawn from many sources — physicians, nurses and laymen. Some had executive ability and experience; many had neither. Superintendents of the larger hospitals who needed assistants developed an apprentice system, whereby after serving for several years a physician, nurse or lay person "graduated" by being called to become the administrator of some other hospital. Although this apprentice system produced many notable administrators, it was inadequate to meet the demand both numerically and educationally. Consequently, beginning around 1920, attempts were made to establish, in existing universities, schools for training hospital administrators — but without success until the University of Chicago opened its School of Hospital Administration in 1934, with support from the American Hospital Association. Now there are at least 7 such schools — at Northwestern, Columbia, Washington University, Duke, Minnesota and Yale.

In September, 1899, the superintendents of 8 of the leading hospitals in the eastern states met in Cleveland to form a hospital superintendents' club. This club, — the first of its kind, — was founded so that its members might convene to exchange information and discuss new technics and ideas. The advantages of such an organization soon became apparent; the membership rapidly increased, and in 1906 the club became the American Hospital Association of the United States and Canada.

Since its establishment, the Association has reflected the growth and development of the hospitals of America. It has also influenced their development in many ways. As the hospital system has expanded, the Association has broadened its scope of activity and its service to members. Annual conventions; committee reports on all kinds of hospital activities;

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the addition of institutional membership to personal membership; the sponsoring of Blue Cross and participation through appropriate committees in Federal and state legislation on hospital matters — these are some of its manifold activities.

Recognizing the need for education in administration, it has encouraged and aided in the establishment of schools, as previously mentioned, and has also conducted institutes for the instruction of administrators and department heads. These institutes are held in many parts of the country several times a year and cover nearly all hospital activities. They approach the equivalent of a postgraduate course, their purpose being to improve hospital administration.

As the American Hospital Association became more of an institutional association, the need for a more individual and personal organization was felt; in 1933 the American College of Hospital Administrators was founded. Its principles of membership are the same as those of the American Medical Association, the American College of Surgeons and similar organizations, with members and fellows ranking according to length of membership, standing and ability. Its objectives were to improve the quality of hospital administration and the standing of administrators and to encourage trustees to select their administrators from among members of the association. It also has conducted institutes for the instruction of members. Thus both hospital associations have shown a lively interest in education.

The last step in the educational field is about to be taken by the School at Columbia. This school will include in its curriculum not only the basic subjects dealing directly with internal hospital administration, such as finance, personnel, dietetics, nursing, hotel and housekeeping and maintenance, but also subjects such as hospital planning, public health, insurance, public relations, legislation, the British National Health Act, vital statistics and other peripheral but related subjects.

Hospital administration has at last been recognized as an important field, involving the competent direction of a complex institution for the benefit of the patient, including the provision and co-ordination of the extensive equipment that permits a surgeon or physician to practice modern medicine. The hospital has become the hub of the health activities of the community. Curative medicine, preventive medicine, public health and medical education all center in the hospital. It is an important factor in our educational system, including instruction in medicine, nursing, social service, dietetics, physical therapy and laboratory technic. The competent hospital administrator must be able to act intelligently in all these fields.

Hospital administrators are drawn from three groups — physicians, nurses and lay persons. In the 6655 hospitals registered by the American Medical Association in 1948, there were 2654 physicians, 2258 registered nurses and 1743 other persons serving as administrators or superintendents. There should always be an appreciable number of physician-administrators, especially in the teaching hospitals. Because of their medical training it is they who should lead and mold the relations of hospitals with public-health work, medical teaching and research. This should not be interpreted to mean that lay administrators may not be equally competent (or even more competent) as individuals to do this, but as a group the physicians should have an advantage in this field. There remain over 4000 hospitals in which the nurse or lay administrator may be better fitted than the physician.

In general the physician seems to fit better in the larger institutions. There seems to be a dividing line, — somewhere about 200 beds, — above which the male administrator functions better and below which the nurse is more effective. Why this is so is not clear, but it seems to be a fact. There are many exceptions; there are men, — physicians or laymen, — in hospitals of less than 200 beds who are doing a good job, and there are some nurses in hospitals of over 200 beds who likewise are good administrators. Probably all or some of these factors contribute: the salary that can be paid; the fact that a nurse can participate in the direction of the nursing service and the training of student nurses; the fact that the larger the number of employees the greater the need for male supervision; and restlessness on the part of a man in a job that does not require all his time or energy. In general the best results are seen with physicians and laymen in the larger institutions and nurses in the smaller ones.

Let us now consider the objectives of hospitals, their organization and some of the ethics and details of hospital administration.*

The primary objective of the hospital is to provide facilities for the care of the sick, to improve methods for the cure, amelioration and prevention of disease and to further the practice of medicine by physicians within the institution. This objective requires a qualified medical staff, a competent administrator, an efficient organization, other well trained personnel and adequate physical facilities.

As secondary objectives, the hospital should encourage research and teaching; it should assist in the advancement of scientific knowledge and fulfill its part in the educational system. The hospital should set an example of ethical practice, co-operate with other hospitals and take an active part in the promotion of health.

The legally constituted governing body is the supreme authority of the hospital and should have full responsibility for its conduct and efficient administration. With the medical staff it forms what is essentially a co-operative relation supported by

*Much of the following is extracted from the Code of Ethics of the American Hospital Association.

the community to carry out the recognized functions of a hospital.

It is the duty of the governing body to select a competent administrator or director to operate the hospital and to carry out the administrative details for such operation. He should be a person of integrity and high professional standards, with satisfactory education, professional training and experience; he should be capable of leadership and able to command the confidence and respect of the governing body, staff, personnel and community. The administrator is in charge of the hospital as the immediate representative of the governing body. As the executive officer of the hospital and the representative of the governing body, he must have the necessary authority and be responsible for the proper management of the hospital, as well as its relations to patients, the public and the staff and personnel, in accordance with the policies adopted by the governing body, so that it may enjoy the full confidence and active support of the community.

He should participate in the deliberations of the governing body and all committees, including staff committees, affecting the administration of the hospital. He should render reports and should present, with his recommendations, those administrative matters requiring consideration by the governing body.

Trustees are responsible for the functioning of a hospital — for financing, for selection of staff and for policies. They should select the administrator, make him responsible for management, give him authority, outline their policies and require him to carry them out and let him alone as to details. This noninterference is essential; too many hospitals have been wrecked by trustee interference. The administrator should keep the board informed of what is going on, what he is doing, of his plans; he should listen to their suggestions and accept their decisions — but it is necessary for discipline and for achievement that he maintain freedom of decision and action concerning the details of running the hospital. All this can be done pleasantly and harmoniously, but it is vital. A meddlesome trustee is like a cancerous growth; such interference is an unnatural condition, and its bad effects will spread.

In his relations with the medical staff the administrator should be sympathetic, understanding and co-operative, with due consideration of the effects of administrative action on individual staff members. He is the liaison between the governing body and the staff and is responsible for carrying out the policies promulgated by the governing body.

A hospital cannot exist without physicians; at present it is difficult for physicians to work without hospitals. Physicians are responsible for the medical care of patients, and one of the functions of a director is to provide the facilities necessary for that care and to co-ordinate the many hospital departments to produce a smoothly operating organization for the benefit of both patient and physician. The administrator must not interfere with medical care. It is his duty, however, to hold physicians to accepted and acknowledged standards and to enforce the policies of the trustees. He should endeavor to have professional problems adjusted by the appropriate professional staff or its committees.

The administrator's relation to hospital personnel should be impartial, tolerant and fair, recognizing the interests of the various groups involved. This includes professional, technical and unskilled employees. He must guard against too intimate relations with any subordinates, as this will inevitably result in relaxation of discipline and accusations of favoritism, whether justified or not. In settling disagreements and complaints he should always remember there are two sides to every question and should hear both sides before reaching a decision.

He should not be an armchair or office administrator; when questions of repairs or alterations are involved he should visit the locality and make his decision on the spot.

The degree of interest that an administrator shows in the comfort and care of patients and the treatment that he accords relatives, friends and visitors will be reflected in the attitude of hospital employees toward patients and visitors.

A successful administrator must keep in close touch with community activities and particularly with community needs. He must maintain a spirit of co-operation with the representatives of other hospitals. Finally, he must realize that his personal and public conduct can never be entirely divorced from the reputation of the hospital that he directs.

An administrator is legally responsible for the proper recording of the admission and discharge of patients, the rendering of innumerable official reports and the safeguarding of the medical records of patients. He must exercise due care in the selection of employees or agents of the hospital. It is his duty to select and oversee the heads of the departments and to co-ordinate the working of these departments. Through the director of nursing whom he has selected he is responsible for the nursing service to patients and, if there is a nursing school, for the school's conformity to high educational standards. Finances, accounting, food, business management, purchase and supply, maintenance of physical plant and many other items are all his or his delegated responsibility.

Dr. Malcolm T. MacEachern lists the following qualifications of a hospital administrator:

He must be well endowed with infinite tact and diplomacy.

He must have firmness tempered with consideration for the weakness of others.

He must be an organizer.

He must be a leader in the community as well as in the institution he administrates.

He must have a sense of the responsibility of his position and of the seriousness of his work, but this must be tempered with a sense of humor.

He must be absolutely honorable and just.

He must be a judge of human nature.

He must be industrious and interested in his work.

He must have administrative ability.

He must be a man of broad education.

His appearance must always be neat and tidy without any tendency toward foppishness.

He must be an educator.

He must be a man of business ability.

He must be a good buyer.

He must be of a mechanical turn of mind.

He must have the ability to work with others.

Admittedly this is idealistic; such a paragon of virtue and ability cannot be found, but we can still "hitch our wagon to a star"; we can still aspire.

All things are relative. The administration of a small community hospital of 50 beds is relatively simple compared to that of a metropolitan teaching hospital of 1000 beds, but the general ethics and principles of hospital administration remain the same, regardless of size.

About twenty years ago the Harvard Business School published a book by Elton Mayo,[2] which contains some statements that are pertinent to hospital administration. Quoting from Brooks Adams, Professor Mayo says:

> Advances in administration seem to presuppose the evolution of new governing classes, since, apparently, no established type of mind can adapt itself to changes in environment, even in slow moving civilizations, as fast as environments change. Thus a moment arrives when the minds of any given dominant type fail to meet the demands made upon them, and are superseded by a younger type, which is in turn set aside by another still younger, until the limit of the administrative genius of that particular race has been reached. Then disintegration sets in, the society sinks back to a level at which it can cohere. To us, however, the most distressing aspect of the situation is that the social acceleration is progressive in proportion to the activity of the scientific mind which makes mechanical discoveries, and it is, therefore, a triumphant science which produces those ever more rapidly recurring changes in environment to which men must adapt themselves at their peril. As, under the stimulant of modern science the old types (i.e. of administrators) fail to sustain themselves, new types have to be equally rapidly evolved. . . . That a modern society can hope to maintain a stable equilibrium in the midst of rapid change only by ensuring that it has amongst its administrators (of both types—governmental and non-governmental), a sufficient number who possess a high order of generalizing mind, a mind which can grasp a multitude of complex relations. But... this is a mind which can, at best, only be produced in small quantity and at high cost. [He proceeds to claim that our educational system has not sufficiently raised its standards]. . . save in science and mechanics, and the relative overstimulation of the scientific mind has now become an actual menace to order, because of the inferiority of the administrative intelligence.

In closing, Professor Mayo states that

> We have too few administrators alert to the fact that it is a human social and not an economic problem which they face. The universities of the world are admirably equipped for the discovery and training of the specialist in science, but they have not begun to think about the discovery and training of the new administrator.

Perhaps hospital administrators do not fall into the category that Professor Mayo describes as possessing "a high order of generalizing mind" that "can grasp a multitude of complex relations," but few can deny that medicine has become a complex science, that hospitals are complex institutions and that administration of the larger institutions does require administrative ability. And it is the larger institutions that set administrative policies.

The establishment of schools of hospital administration by so many universities can be regarded as a hopeful sign and as recognition on their part of the need of thinking about "the discovery and training of the new administrator."

Hospitals are destined to play an increasingly important role in the development of medicine and public health in the coming years; the future of medicine and hospitals is inseparably connected with the character, ability and intellectual qualities of the present and succeeding generations of hospital administrators.

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MEDICAL INTELLIGENCE

A NEW SELF-RETAINING ELECTRO-CARDIOGRAPHIC ELECTRODE*

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CURRENT advances in unipolar-lead electrocardiography make it necessary to take leads from regions of the chest and back that are not covered by the six routine precordial leads.[1] For this purpose the currently used rubber chest strap is no longer sufficient for adequate support of the precordial electrode. Furthermore, the strap necessitates considerable time and effort for its application and cannot be used in patients unable or forbidden to move in bed. The recently improved suction electrodes[2] have the disadvantage of being difficult to keep in place in very lean persons with protruding ribs. Moreover, none of the electrodes at present in use allow the registration of leads from the back in the recumbent position. Another disadvantage of these electrodes is that in the presence of marked precordial pulsation their mass causes the pressure that they exert against the chest wall to vary with the heartbeat; this may lead to rhythmic artefacts that distort the T wave and RST segment.[3] In order to avoid these difficulties, I have developed a small self-retaining electrode, which has the advantage of ease of application and maintenance and freedom from base-line shifts.

The electrode consists of a disk of stainless steel 2/1000 inch thick and about 3 cm. in diameter; at one point on its periphery it has a tapering extension that is used for attachment of the wire leading to the electrode cable. The electrode can be cut out of a sheet of stainless steel with ordinary scissors. The purpose of the extension is to eliminate any contact with electrode paste of the junction between the electrode and the wire leading to it; such a contact sets up electromotive forces between the two metals and causes drifting of the base line. Another reason for the extension is that it is difficult to solder the wire to stainless steel, and a mechanical junction with the tapering end of the electrode is much easier. The junction is firmly wrapped with insulating adhesive tape (the black plastic variety is best). The wire best suited for connection to the standard electrode cable is Belden indoor aerial wire. This plastic-coated multiple-strand wire is sufficiently light and flexible to prevent any pull on the electrode and yet rugged enough to withstand long use without breakage. The wire is about 2 feet long and has a small battery clip at its distal end, by means of which it is clipped onto the contact at the end of the precordial electrode cable (Fig. 1).

The stainless-steel-foil electrode and the wire attached to it are so light that the electrode remains indefinitely in contact with any part of the chest by adhesion to the electrode paste, which has been applied to the skin. It is ideally suited for exploratory precordial electrocardiography, as it takes less than a second to change its position. The electrode is so thin that it can be applied to the back of the recumbent patient without causing him discomfort. Its small size, as well as the flexibility of its connecting wire, makes it possible to register the routine six precordial leads, through the front opening of the shirt or blouse without necessitating the patient's undressing. Owing to the same factors, the electrode always exerts constant pressure on the chest, even in the presence of precordial pulsations or labored breathing, hence the base line remains stable. Contrary to some writers' statements,[3] I have found that stainless steel causes the smallest base-line drift; it also has the advantage that it does not oxidize or corrode and does not need to be washed after use, as the electrode paste falls from it when dry.

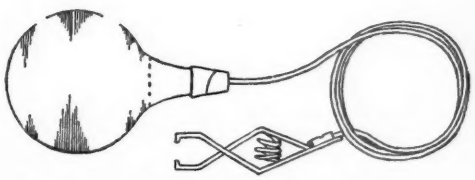

FIGURE 1. *Self-Retaining Electrocardiographic Electrode.*

SUMMARY

A new self-retaining precordial electrode made from stainless-steel foil is described. It is characterized by ease of application and upkeep and by freedom from base-line shifts and other artefacts.

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RUBELLA IN PREGNANCY

ONCE called a "nuisance rather than a disease," German measles is anything but that for the expectant mother who contracts the infection in early pregnancy. Yet, even ten years after the teratogenic capacities of the virus have been established, the precise risk cannot be stated — so rare are cases among adult females at a selected stage of gestation, so variable are the expressions of maternal infection in the infant, so cumbersome is the task of case finding, follow-up study, classification of defect and centralization of data. It is doubtful, however, that the risk of serious malformation is more than 15 per cent even at the first, crucial trimester of pregnancy, and it may prove less.

Although there is an additional risk — perhaps as large as 20 per cent — of spontaneous abortion, that threat poses a less serious problem psychologically and sociologically. There is merely the medical problem of aiding the mother in labor. The parents start again with the slate wiped clean, so to speak. On the other hand, the pregnant mother who has had rubella in the first trimester and feels life continuing within her for months must wonder whether her 15 per cent risk will bring to the infant a slight defect in hearing, significant deafness or blindness, or worst of all the disintegration of the central nervous system that manifests itself as "mental retardation." For her the outcome of pregnancy is a gamble — *rouge* or *noir*, *noir* representing disaster for the infant.

It is curious that in the ten years since Gregg[1] demonstrated the crippling power of rubella, no effective program has been worked out to control the possibility of infection during pregnancy; the solution to the problem is simple — for young girls to "get the disease and get it over with" before they undertake the responsibilities of marriage and motherhood. As a rule immunity is lifelong, a second attack of rubella being rarely observed. This is evidenced by the age distributions of reported cases, and the fact that rubella is one of the "immunizing diseases of childhood" is confirmed by everyday experience of physicians and nurses who, though exposed several times a year to patients, do not develop the disease a second time. Until the day comes when active immunization from having had the disease is regarded as seriously by physicians as whooping cough, diphtheria and tetanus prophylaxis, the predicament of the occasional patient's contracting rubella in pregnancy will continue to plague obstetricians. For such patients a statement of risk is needed, but unfortunately the data are altogether too fragmentary to permit a clear formulation of the risks.

Provisional figures given (Table 1) show that no physician is justified in stating categorically that rubella in the first trimester of pregnancy is always associated with a bad prognosis. More such data are needed, and they are sought from readers of this department. As Logan[7] has stressed, reports are of greatest value if selection of cases is made before the child is born. Otherwise there may be a tendency to report tragedies and to omit reporting of unaffected infants. Thus it is essential that the outcome of all cases of rubella in pregnancy occurring in any one practitioner's experience be reported.

TABLE 1. *Effect on the Fetus of Rubella in Pregnancy, Classified According to Time of Infection.*

SERIES	FIRST TRIMESTER			SECOND AND THIRD TRIMESTERS		
	TOTAL CONCEPTIONS	STILLBIRTHS	CONGENITAL MALFORMATIONS	TOTAL CONCEPTIONS	STILLBIRTHS	CONGENITAL MALFORMATIONS
Fox and Bortin[2]	9	1	1	2	0	0
Aycock and Ingalls[3]	2	0	1	1	0	0
Ober, Horton and Feemster[4]	22	6	5	32	3	3
Grönvall and Selander[5]	13	2	0	15	1	1
Hill and Galloway[6]	5	1	0	4	0	0
Totals	51	10 (20%)	7 (14%)	54	4 (7%)	4 (7%)

If readers of this article will undertake to inform the editors of the outcome of any cases of rubella in pregnancy, *no matter at what stage it occurs*, the results will be assembled in a later communication to be published in this department of the *Journal*.

The following information is needed for all cases of which there is knowledge — preferably before the baby is born*:

1. Physician's name and address.
2. Mother's name (will be held confidential) or initials.
3. Mother's age.
4. Date of last menstrual period.
5. Date of onset of rubella.

The baby's condition:

1. Birth date.
2. Stillbirth.
3. Normal.
4. Defective.
   (a) Primary defect.
   (b) Associated defects.

*Check one:

Information about baby will be sent later.
Information about baby already known.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

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CASE 38301

PRESENTATION OF CASE

A thirty-five-year-old woman was admitted to the hospital because of pain and stiffness of the fingers and hands.

Five months before entry the patient had the onset of "spells" during which her fingers first turned white and then became blue and mottled; these occurred every day and, although often precipitated by cold or emotional factors, also occurred independently of either of these factors. "White pills" prescribed by her physician gave some temporary relief, but then she began having swelling, tightness, pain and stiffness of the hands and fingers, which felt hot and sweaty. About a month prior to entry her feet also became swollen, stiff and painful. Since the onset she had had progressive extreme fatigue, which was especially severe in the month before admission. For a month before admission she noted that after she stayed in one position for any length of time her knees, hips, back, elbows and shoulders felt stiff and painful on motion. She had had profuse night sweats for the two months prior to entry.

Three years before entry she struck her head on a door but did not lose consciousness. Thereafter she had frequent severe headaches, and soreness in the area of the injury. Roentgenograms of the skull allegedly showed a small fracture, and a pneumoencephalogram was normal. Because of persistence of the headaches, irritability, nervousness and fatigue she was treated by a psychiatrist. Two and a half years before admission she had three attacks of "pleurisy" in the left side of the chest, the first of which lasted two weeks and was associated with fever. Roentgenograms of the chest were allegedly normal. Two years prior to entry and three months after a normal pregnancy and delivery, she developed jaundice and remained in bed for three months. She was quite well after this, except for the headaches and irritability. One year before admission, when she learned that her youngest child was a "Mongolian idiot," she became quite depressed, irritable and listless. Because these symptoms persisted she was given electric shock therapy over a three-week period, six months prior to entry.

Her appetite had remained fair and there had been no weight loss. There had been slight exertional dyspnea and ankle edema for three months prior to entry. There had been no cough, hemoptysis, change in bowel habits, urinary symptoms or skin rashes or nodules.

Physical examination revealed a thin, pale woman. There were no rashes or skin nodules. The thyroid gland was not enlarged. The lungs were clear. The heart was of normal size. There were Grade I apical and basal systolic murmurs. The sounds were of good quality, and the aortic second sound was louder than the pulmonic. Examination of the abdomen was negative. The peripheral arteries seemed normal. The fingers were slightly swollen, warm and slightly moist and had a normal color when first seen. After a discussion of her Mongolian child during which she became quite upset, the fingers became mottled and those of the right hand quite cold and white. The grip was good. There was some slight swelling and mottling of the feet, which were cold and moist. There was minimal pitting edema of the ankles. All other joints appeared normal.

The temperature was 99°F., the pulse 95, and the respirations 20. The blood pressure was 120 systolic, 70 diastolic.

A catheter specimen of urine had a specific gravity of 1.024 and was normal. Examination of the blood showed a hemoglobin of 12.0 gm. and a white-cell count of 17,400, with 84 per cent neutrophils; the red cells, on smear, were achromic and varied slightly in size; the platelets were normal. An erythrocyte sedimentation rate was 1.05 mm. per minute, and a hematocrit was 37 per cent packed red cells. No lupus-erythematosus cells could be demonstrated. The total protein was 6.00 gm.,

with an albumin-globulin ratio of 1.2, the nonprotein nitrogen was 26 mg., and the fasting blood sugar 87 mg. per 100 cc., and the serum bilirubin and bromsulfthalein test were within normal limits; the prothrombin time was 15 seconds (normal, 14 seconds). The stools gave negative guaiac reactions. One blood culture was negative, whereas a second grew out nonhemolytic streptococci. Agglutination tests for typhoid, paratyphoid and undulant fever and a heterophil-antibody test were negative. The roentgenograms of the chest showed a slight patchy density in the inferior lingular segment of the left upper lobe, with a suggestion of a slight reduction in size of the lingular segment; the diaphragm, heart and vessels were not unusual. A Graham test was normal. A barium-swallow examination suggested slight atonicity of the esophagus. A gastrointestinal series was negative. An electrocardiogram was normal. The vital capacity was 2.2 liters (66 per cent).

After the first twenty-four hours in the hospital the patient had a daily temperature rise up to 101 to 103°F.; the pulse rate was between 80 and 90, and the respirations within normal limits. She continued to have the changes in the hands and feet, and weakness. On the tenth day she complained of pain in the knees; examination showed some quadriceps-muscle weakness, questionable soft-tissue thickening but no evidence of effusion in the knees, and tenderness and pain in other joints, over bony prominences and in the muscles generally. She complained of a "tightness" in the throat on swallowing, of epigastric and substernal pain, usually while eating, and of pain and a sandy feeling in the eyes. A chest roentgenogram on the eighteenth day showed the changes noted before to be a little less marked. Repeat examinations of the blood showed the hemoglobin and white-cell count to be of the order of that on admission. The symptoms continued unchanged, but the patient became progressively more ill. The only changes in physical findings were a Grade III pulmonary systolic murmur and accentuation of the second pulmonary sound. On the fortieth day a biopsy from a tender area of the left gastrocnemius muscle showed no diagnostic abnormality. In the afternoon of this day she developed a feeling of constrictive pressure across the lower chest accompanied by difficulty in breathing; a slight cough had been present for the preceding twenty-four hours. She was very apprehensive and pale. The pulse was weak and rapid, and the respirations were rapid. The blood pressure was 100 systolic, 80 diastolic. The heart seemed slightly enlarged. The pulmonic second sound was definitely louder than the aortic, and there was a diastolic gallop. There were medium and coarse rales throughout the lungs. X-ray films of the chest showed pulmonary edema in both lungs, with accentuation of the vascular markings. A small amount of fluid was present in the costophrenic sinuses. The heart lay transversely and was prominent in the region of the left ventricle. Morphine given intramuscularly promptly relieved the discomfort, but the patient remained pale, cold and clammy and eight hours later had a blood pressure of 66 systolic, 56 diastolic. She became moribund, with gasping respirations and an unobtainable blood pressure, and died about an hour later, on the forty-first day.

Differential Diagnosis

Dr. Alfred Kranes*: Were lupus-erythematosus cells looked for more than once?

Dr. J. Wallace Zeller: No.

Dr. Kranes: "One blood culture was negative, whereas a second grew out nonhemolytic streptococci." That is the only reference in the protocol to a positive blood culture. I wonder how many were taken and whether organisms were found more than once?

Dr. Zeller: A number of blood cultures were done, and no organisms were found.

Dr. Kranes: I hope, Dr. Wyman, that you were not responsible for the fence-riding x-ray reports, all of which "suggested" some abnormality.

Dr. Stanley M. Wyman: Not guilty.

Dr. Kranes: I once made a collection of equivocal statements in patient's records; I think the most outstanding one described the scleras as having a "questionable subicteroid tint."

It seems to me that the diagnosis one arrives at with this patient will depend in no small measure on the significance one attaches to the series of apparently unrelated events preceding the onset of Raynaud's disease and on how one explains the manner of death. The unrelated happenings I refer to are the headaches, the attacks of pleurisy and the jaundice that occurred a year and a half before the symptoms in the hands began. I like to think of these as having nothing to do with the present illness, largely because I find myself unable to fit them into the over-all picture. The headaches seem like the type that one might expect to follow a head injury in certain emotionally unstable people, which apparently this patient was, and I find it difficult to relate them to subsequent developments. The pleurisy, which appeared next, could have been part of what later developed, although without more knowledge about the nature of the pleurisy, it is difficult to be certain. The jaundice, which followed the pregnancy by an interval of three months, forces one to consider homologous serum hepatitis. The protocol refers to the pregnancy as a normal one. I do not know whether a normal pregnancy includes the giving of blood or plasma. At any rate, she probably had many other injections. Since I do not see how I can fit that into the rest of the picture, I am going to dismiss it as an unrelated disease, particularly in view of the fact that during the

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present admission, tests of liver function were all perfectly normal.

It may seem odd to discuss a patient's death before discussing the nature of her illness; yet I think it may be of interest to reverse the process here. This patient obviously died of either massive pulmonary infarction or some accident within the heart, such as an obstructed coronary vessel or rupture of a cusp, valve leaflet or papillary muscle. On the data presented, there is not enough information to decide which of these occurred. The sequence of pain in the calf and the manipulation that must have taken place during the biopsy, followed within a few hours by chest symptoms and sudden collapse, argues strongly in favor of a massive pulmonary embolus. The x-ray films lend no support to that conclusion, but I would not expect them to. The intracardiac accidents can very readily be fitted into the picture of an underlying disease. I shall return to that in a few moments. My personal belief is that her death was the result of a massive pulmonary embolus.

Having abstracted, from this history, the headaches, the pleurisy and the jaundice and having assumed that the patient's death was in no way related to the underlying disease, I am left with essentially a five-month history of joint pains, Raynaud's disease, fever and leukocytosis. I wondered, as I reflected about this patient, whether she had a disease that an untimely death prevented from developing in all its manifestations. If she had not died of a massive pulmonary embolus, the more characteristic features of this disease might have subsequently made themselves evident. Dr. Walter Bauer is fond of saying of these patients, "Time will tell"; perhaps if enough time had been allowed this patient, it might have told. Of the diseases about which this is most characteristic, the most common are the so-called group diseases, sometimes called the collagen or the connective-tissue diseases. These consist of lupus erythematosus, polyarteritis nodosa, dermatomyositis and scleroderma. Which of these diseases to call suspect is indeed a problem. One would be safer if one merely stated that this patient was suffering from one of the group diseases and let it go at that, but the unwritten rules of this session impel one to make a more specific diagnosis even though the evidence does not warrant it.

In the information supplied here I find little on which to make the diagnosis of lupus erythematosus. The usual manifestations of the disease were lacking. The patient had no rash, no leukopenia and no significant anemia; she did have joint involvement and fever. Although it is true that lupus erythematosus may be present in the absence of a rash, with a leukocytosis, and without anemia, I do not see how one is permitted to make such a diagnosis clinically.

Dr. Zeller: Several of the examinations revealed a small amount of albumin and occasional red cells in the urine.

Dr. Kranes: Dr. Zeller is leading me on. I meant also to say that the patient gave no evidence of renal disease, but apparently that is not true. Sir William Osler once wrote a paper on the advantages of slight albuminuria and a few red cells in the urine. I think the findings would fit in with any long febrile illness.

One suggests polyarteritis as a diagnosis with a great deal of diffidence, but in this situation it must be seriously considered. Once again the customary manifestations of the disease were not present — if there are any customary manifestations; at least she did not have peripheral neuritis or abdominal pain. She did have fever, but no renal disease of any significance. I shall have to reject polyarteritis nodosa for lack of adequate evidence although I realize it may have been present. The same conclusion is true of dermatomyositis. The patient had no skin rash; the muscle weakness described is rather impressive, but I do not know whether clinically the weakness was as great as it sounds in the record.

Dr. Zeller: It was very definite.

Dr. Kranes: So that one would have to consider dermatomyositis seriously. The muscle biopsy, however, showed no abnormality. I am not sure whether the muscles all over the body are likely to show lesions. The patient had the disease for five months and had marked symptoms; I suspect that it would have been at the stage in which the lesion would be found histologically.

If I must commit myself, I find myself attracted to scleroderma rather than to the other members of the group. She had Raynaud's disease, which is a very common finding in scleroderma; she had no skin lesions, unfortunately, but the stiffness and difficulty in moving the joints after she had been in a particular position are suggestive of some induration of the subcutaneous tissue even though none was described on physical examination. The x-ray reports, into which one may read anything he wishes, also lend a little support to the diagnosis of scleroderma.

May I see the x-ray films, Dr. Wyman? I am more interested in the esophagus than any of the other films.

Dr. Wyman: The esophagus is not too well shown. The evidence about the esophagus that I do have is that it is not at all unusual. It seems to be fairly normal in width. I cannot tell anything about its activity, however, since that was a fluoroscopic observation. The changes in the lingula (seen lying anteriorly) may be any form of chronic disease, probably of some duration. The lung fields are not particularly unusual otherwise. The heart shadow is not enlarged. The spleen and, as far as I can tell, the liver are not enlarged. The stomach

and duodenal cap and loop are not remarkable. The final film shows what I think is quite typical pulmonary edema.

DR. ZELLER: Would you say the lingular change is more than suggestive?

DR. WYMAN: I think there was something in the lingula, such as an old bronchiectasis.

DR. KRANES: You mean it has nothing to do with the present illness?

DR. WYMAN: I cannot fit it into the present illness. I was trying to find some changes in the peripheral lung fields, but I cannot be sure of anything.

DR. KRANES: I am left more or less where I started. I merely want to point out that scleroderma can produce the abnormalities described. Would you say the lung changes were inconsistent with a diagnosis of scleroderma?

DR. WYMAN: I should like to see a more diffuse process; this is too localized. She may have had some aspiration pneumonitis if there was difficulty with the esophagus. That is another possibility.

DR. KRANES: Scleroderma would also explain the esophageal symptoms. What bothers me considerably about making the diagnosis of scleroderma is the absence of skin lesions and the presence of such a high temperature. I was not aware that a patient with scleroderma could run this degree of fever for so long a period. Not knowing that this was Dr. Zeller's patient, I asked him yesterday whether a patient with scleroderma could run such a fever for so long; he assured me that one could. I should also mention that patients with one of the group diseases occasionally have a verrucous nonbacterial endocarditis. It is more commonly seen in patients with disseminated lupus erythematosus, but it has also been found in patients with other members of the group. Conceivably, this final episode may have been a ruptured papillary muscle or cusp. If I were faced with the care of this patient scleroderma would be the diagnosis that would seem to me most likely.

In the remaining minute or two I shall mention other more remote possibilities. Rheumatic fever occurred to me, but there are so many objections to it that I shall not go into them. The one positive blood culture and the continued fever seriously raise the question of bacterial endocarditis, which could explain a great deal of this patient's illness, including her death. If she had bacterial endocarditis she may have died as a result of a small vegetation occluding a coronary artery. But there was only one positive blood culture. I would gather from Dr. Zeller's statements that he did not think the patient had bacterial endocarditis — at least, she was not treated for it, and she had no petechiae, no clubbing and no enlarged spleen.

In any prolonged fever, lymphoma and other malignant lesions must be considered, but there certainly was no evidence for them. Hypernephroma can also produce prolonged fever. Dr. Wyman just made me think of another possibility. With localized disease in the left lower lobe and pain in the joints, one has to think seriously of carcinoma of the bronchus, with acute pulmonary osteoarthropathy. I have never seen it without clubbed fingers. I shall have to choose scleroderma as the probable diagnosis.

DR. ZELLER: The travail that Dr. Kranes went through for half an hour was experienced by us for about a month. This was an interesting patient about whom a good deal could be said. She was originally sent to one of the surgeons for a sympathectomy for Raynaud's disease. The surgeon was extremely canny and recognized that something else might have been going on that had Raynaud's syndrome as one of its manifestations. He suspected valvular heart disease and asked for a cardiology consultation. The cardiologist went over the matter very carefully, considering many of the conditions that have been mentioned here, and leaned strongly toward scleroderma. When I saw the patient, I thought any of the group diseases, including scleroderma, was a definite possibility.

I am interested that you did not mention rheumatoid arthritis, Dr. Kranes.

DR. KRANES: I certainly should have.

DR. ZELLER: We considered rheumatoid arthritis because of the history of pleurisy and the joint manifestations. She complained of severe knee pain, and at times the knees felt hot. It would be most unusual, however, to have arthralgia without more signs of joint inflammation as a manifestation of clear-cut rheumatoid arthritis. I favored lupus erythematosus. The patient was examined carefully day after day for localized signs; as far as I was concerned, the only definite finding was the x-ray change in the lung, which was a very tenuous thread to hold on to to make any type of diagnosis. I did not take care of her during her last week of life. I had thought of doing a muscle biopsy about the time I went away. Up to that time she had had no localized muscle pains whatever. She had had pains involving the whole lower limbs, but I did not think there were signs that warranted electing one particular site for a biopsy.

DR. JAMES C. WHITE: I saw this patient four months before she came into the hospital. She was originally sent to me with the diagnosis of Raynaud's disease. Of course, Raynaud's phenomena may be a preliminary of any kind of disease compressing or constricting the arteries like scleroderma or dermatomyositis. At the time she had very little to suggest scleroderma. The dyspnea began later — three months before admission. I sent her to Dr. Robert R. Linton because I have stopped taking care of patients with peripheral vascular disease. From past experience I have become very allergic to this group of diseases because a number of times I, and other surgeons, have done sympathectomies on persons who appeared to have Raynaud's disease

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only to find that they progressed to scleroderma. Under these circumstances operation has either made the condition worse or produced no improvement. It is of interest in the hospital history to note that, as she was talking about her Mongolian child, the patient became extremely upset and developed striking vasospastic changes. Dr. Stanley Cobb[1] brought out in his book that emotional upsets may precipitate intense vasoconstriction in certain persons with Raynaud's disease.

DR. WILLIAM CLARK: I had thought the clinical picture was more consistent with myocardial infarction. Dr. Walter Bauer and I had taken the patient over from Dr. Zeller while he was away. When Dr. Bauer first saw her he favored the diagnosis of polyarteritis, and for that reason the biopsy was proposed. At the time of the terminal episode we reasoned that she had had polyarteritis and had a myocardial infarct on the basis of small-vessel occlusion.

DR. EDWIN O. WHEELER: When I first saw her, I favored scleroderma because of the change in the esophagus and lungs as well as in the extremities.

DR. CHESTER FRAZIER: If scleroderma can occur without scleroderma, lupus erythematosus might occur without erythema.

CLINICAL DIAGNOSIS

Polyarteritis nodosa.

DR. KRANES' DIAGNOSIS

Scleroderma.
?Massive pulmonary embolus.

ANATOMICAL DIAGNOSES

Platelet thrombosis.
?Lupus erythematosus.
Myocardial infarction.

PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The autopsy here showed no evidence of primary skin or muscle disease grossly or microscopically. The heart was normal in size and weight, but when it was sectioned, the outer third to half of the myocardium of the left ventricle was obviously infarcted. This was a very interesting picture in that the infarction did not involve any of the inner half of the wall of the ventricle as it does ordinarily; it was a band of recent infarction in the outer third. The coronary arteries, which we examined very carefully, were normally patent and thin, and gave no evidence of sclerosis. There was not a major coronary thrombosis to account for the myocardial infarction, and it would not be expected from the distribution of the infarction. The lungs showed moderate pulmonary edema. At the time of autopsy we were unable to make any diagnosis other than myocardial infarction, cause undetermined.

The sections of the heart explained the infarction. In some areas there were areas of healing, so that the process has been going on certainly for a week if not longer. We looked in the areas of infarction for occlusions and found many of the smaller arteries and arterioles not only within the areas of infarction but also in normal muscle occluded by thrombi. The walls of some of the vessels showed a smudginess, which is evidence of necrosis of the wall, but in many of the occluded vessels we found no necrosis of the arteriolar wall. These obvious thrombi in the vessels were not made up of fibrin, as shown by special stains; we assume that they were platelets. This is an appearance similar to that seen in the so-called platelet thrombosis or thrombotic thrombocytopenic purpura, which has also been called thrombocytic acroangiothrombosis,[2] a condition that this patient did not have clinically. There was no evidence of purpura or thrombocytopenia. Similar platelet thromboses were found in the afferent arterioles of the kidneys, in one section of the adrenal gland and in one of the pancreas. There was no reaction surrounding the necrosis, so that I think we can fairly well rule out polyarteritis nodosa, in which there is always a cellular reaction along with the necrosis. On the other hand these findings, without the thrombi, have been described in disseminated lupus erythematosus — for example, the cases of lupus erythematosus reported from the Mt. Sinai Hospital[3] showed smudginess, the so-called fibrinoid necrosis without thrombi, in the vessel walls of various organs. The spleen showed quite prominently periarterial fibrosis — an appearance that has so often been seen in disseminated lupus erythematosus.

The findings in this case are therefore a combination of those seen in lupus erythematosus and in thrombotic thrombocytopenic purpura associated with a platelet thrombosis. There has been some evidence that these two conditions are allied. In a recent paper[4] 2 cases having features of both lupus erythematosus and platelet thrombosis clinically and anatomically were reported. Also, Orbison,[5] in Cleveland, who has done some interesting studies on vessel changes in a clear-cut case of platelet thrombosis, made a model of the arteries and found aneurysms that he said indicated necrosis of the vessel walls. He believes very strongly that the disease, platelet thrombosis, is not a primary condition but is secondary to changes in the arterioles. The findings in this case certainly would bear that out — it is a secondary manifestation of the disease of the arterioles. Perhaps, too, the condition of platelet thrombosis may be added to the list of group diseases.

We examined the brain quite carefully. Adams,[6] who has made a study of the cerebral changes in the cases of platelet thrombosis at the Boston City Hospital, informs me that there were no changes

in the arteries of the brain in the case under discussion.

DR. ARTHUR S. PIER, JR.: Did the patient receive cortisone or ACTH at all?

DR. ZELLER: Not under our care. I should like to have Dr. Clark tell us what result he would expect from steroid therapy.

DR. CLARK: We are dealing with a new situation from a histologic point of view, and it would be hard to say what to expect. Treatment of scleroderma and polyarteritis nodosa has been rather disappointing although some physicians have had more success than others. One might expect the ACTH to control the fever and perhaps to prolong life. I do not know that we could have prevented this rather mysterious type of lesion.

DR. ZELLER: I was referring to the phenomenon of thrombosis as influenced by steroid therapy.

DR. CLARK: Thrombotic phenomena frequently occur during steroid therapy, and for that reason cortisone or ACTH might be contraindicated.

DR. PIER: Dr. Gardner, at the Peter Bent Brigham Hospital, has had several cases of so-called Moschcowitz syndrome or platelet thrombosis that have responded dramatically, at least for a short time, to steroid therapy.

DR. KRANES: Did you find anything in the left lower lobe?

DR. CASTLEMAN: There was some organizing and organized alveolar exudate, which must have been due to a previous infection. The rest of the lung showed severe edema.

DR. CLARK: Dr. Castleman, if a muscle that was clinically involved were selected for biopsy, the chances are that the changes of dermatomyositis would have been found, provided that the patient had that disease.

DR. CASTLEMAN: Yes.

DR. CLARK: In this patient we selected the muscle with the most involvement. She had pain in the calf muscles without signs of thrombophlebitis. We thought she did have myositis.

DR. CASTLEMAN: The muscle from the biopsy and the muscles from about a dozen sites at autopsy showed no vascular disease.

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CASE 38302

PRESENTATION OF CASE

A seventy-four-year-old man was admitted to the hospital in a semicomatose condition.

Three months prior to entry the patient developed weakness of the right hand, but retained good motor power at the elbow and shoulder; there was no diplopia, headache, vomiting, convulsions or difficulty in walking or talking. On examination his physician noted hypertension but nothing else of significance. Other than difficulty with shaving and feeding himself there was nothing of note until one week before admission, when a fairly severe headache, located in the vertex and occiput, developed. On the morning of admission, shortly after getting out of bed, he walked a few steps and then fell to the floor. He did not have convulsions or completely lose consciousness, but thereafter he was stuporous, restless and almost completely aphasic and did not voluntarily move his left side.

He had been in excellent health prior to the present illness. Ten years before entry, on routine examination, asymptomatic diabetes mellitus was found, which was well controlled by diet alone. There had been no dyspnea, reduced exercise tolerance, anorexia, weight loss, change in bowel habits or periods of confusion. For some years he had had nocturia of three or four times.

Physical examination revealed an obese, semistuporous man who could form only a few words. There were multiple purpuric spots in linear distribution in the skin of the extremities, chest, and face; these were both single and confluent, flat, nonblanching, rounded, dark-red macules measuring 1 to 3 mm. in diameter. The eyes rolled from side to side, and the pupils reacted sluggishly to light. There was flattening of the nasolabial fold on the left, with drooping of the left side of the mouth. He could swallow, but gag reflex was absent. The neck was supple. There was a flaccid paralysis of the left arm and leg. The right hand was weak, but he could move the right arm and leg. The deep tendon reflexes were slightly decreased on the left. The Babinski sign was extensor on the right and questionably extensor on the left. Coarse rales were present at the base of the right lung. The heart was enlarged with the point of maximum impulse 11.5 cm. to the left of the midsternal line; there was a Grade II precordial systolic murmur. The pulmonic second sound was equal to the aortic. The liver was not palpable but could be percussed two fingerbreadths below the right costal margin. The prostate was enlarged to two or three times normal size.

The temperature was 99.8°F., the pulse 120, and the respirations 25 and of the Cheyne-Stokes type. The blood pressure was 200 systolic, 110 diastolic.

The urine had a specific gravity of 1.016 and gave a negative reaction for sugar; the sediment contained

5 to 10 red cells per high-power field. Examination of the blood showed a white-cell count of 16,500, with 82 per cent neutrophils, and a hemoglobin of 16.3 gm. The blood platelets appeared to be reduced on examination of a blood smear. The nonprotein nitrogen was 29 mg., and the bilirubin 0.5 mg. direct and 0.8 mg. total per 100 cc.; the sodium was 138.3 milliequiv., the chloride 100 milliequiv., and the potassium 4.0 milliequiv. per liter. A prothrombin time was 16 seconds (normal, 14 seconds). A tourniquet test produced 36 petechiae in an area 2 cm. square. The bleeding time was 5½ minutes (Duke method). A blood culture grew abundant colonies of *Staphylococcus aureus* in one flask and *Staphylococcus albus* in a second. A culture of some of the petechiae showed no growth. Guaiac tests on the stool and vomitus were positive. A lumbar puncture revealed a spinal-fluid pressure equivalent to 380 mm. of water, normal dynamics and crystal-clear fluid; the fluid contained 80 red cells per cubic millimeter and 45 mg. of protein and 110 mg. of sugar per 100 cc. An electrocardiogram showed a normal rhythm, with a PR interval of 0.18 second and a QRS interval of 0.08 second. There was normal voltage and axis. The ST segment was slightly elevated, and the T waves were diphasic in Leads 2, 3, AVF and V_6; the ST segment sagged slightly in Leads 1 and AVL; the Q waves were deep in Leads 3 and AVF and small in Lead 2; the T waves were tall in Leads V_2, V_3 and V_4.

The patient continued to be semistuporous and had a temperature varying between 100 and 104.2°F. He was treated with intramuscular injections of penicillin. A few more petechiae appeared on the extremities. An indwelling bladder catheter was inserted, after which the urine was grossly bloody. Lumbar puncture on the third day showed a spinal-fluid pressure equivalent to 150 mm. of water and slightly xanthochromic fluid containing 65 cells, of which 4 were white cells, and 76 mg. of protein per 100 cc.; a culture showed no growth. Numerous repeated blood cultures showed no growth. A white-cell count on the fifth day was 24,400, with 82 per cent neutrophils. The patient's condition gradually deteriorated; he became totally unresponsive, with flaccidity of all limbs. He died quietly on the seventh day.

Differential Diagnosis

Dr. Reed Harwood*: The first point of significance in the record is the story of weakness of the right hand that developed three months before the patient was admitted to the hospital. I naturally wonder whether that development was a part of the final illness or was a totally unrelated episode. In a man of seventy-four with hypertension, one might simply ascribe that weakness to a small infarct in the left cerebral cortex.

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On physical examination he did not have signs of meningeal irritation. He had coarse rales at the base of the lungs. Were any chest films taken?

Dr. Robert E. Scully: None were taken.

Dr. Harwood: Aside from the neurologic findings, which I shall discuss later, the physical examination was not remarkable. One might find similar physical signs in any man of seventy-four years who was acutely ill. The patient may have had a heart murmur for a long time. The rales may have been the beginning of a pneumonia as a result of an acute illness.

What information do I get from the laboratory tests? The urine showed no sugar, but the sediment contained some red cells. In a man who has a fever, particularly at this age, a few red cells in the urine are of no great significance. He had an elevated white-cell count and an estimated reduction in platelets in the smear. I do not know how much emphasis should be placed on that. The nonprotein nitrogen was normal, as was a series of blood chemical determinations, which do not seem clearly indicated in this case. There was one important omission — namely, there was no record of blood sugar determinations. An acutely ill diabetic patient should have a blood sugar test even when he has no glycosuria; the finding is sometimes quite surprising. The tourniquet test produced 36 petechiae. How important is that? I have done that test many times on diabetic persons and found it positive to this extent, as well as many times in the older diabetic patients and in some of the young ones with severe diabetes. The guaiac tests showed the presence of occult blood in both the stool and vomitus. I am inclined to think that the occult blood was part of an acute illness rather than due to some lesion in the gastrointestinal tract. The electrocardiogram I shall pass over as showing minor nonspecific changes. A very interesting finding was that one blood culture grew out abundant colonies of *Staph. aureus*; a very disturbing finding was that the other culture grew out *Staph. albus*, which is a common contaminant of blood cultures, but an abundant growth of *Staph. aureus* must be taken extremely seriously. In fact I feel obliged to base my diagnosis on this finding. I believe the patient had a staphylococcal septicemia.

As I read the record, I thought first of a cerebral hemorrhage in an old man with hypertension, or possibly a massive cerebral thrombosis. I also believed I had to consider a subdural hematoma and a brain tumor, perhaps with hemorrhage into it. When I read about the blood cultures that grew out *Staph. aureus*, I had to consider a brain abscess as another diagnostic possibility. The increased spinal-fluid pressure confirms the suggestion that the patient had an expanding brain lesion. The 81 red cells in the fluid I would interpret as showing no profound cerebral hemorrhage or at least no major hemorrhage into the subarachnoid spaces.

The patient's course in the hospital was one of sepsis, with a swinging septic temperature ranging between 100 and 104°F. A high temperature is not uncommon in a patient with any brain lesion severe enough to produce stupor. He was treated with penicillin — that may be why cultures from the petechiae failed to grow staphylococci. Only a few more petechiae appeared on the extremities; that may mean that the septicemia was controlled by the penicillin. On the third day a repeated lumbar puncture showed that the spinal-fluid pressure had dropped; that may have been due to the reduction of edema around the brain abscess as a result of penicillin therapy. That repeated blood cultures were negative can also be attributed to the penicillin.

If the *Staph. aureus* blood culture reflected a staphylococcal septicemia, what was the source of this infection? The two commonest sources of brain abscess are infection of the middle ear and a suppurative pulmonary process. This patient had no evidence of sinusitis, and I assume that the examination of the ears was negative. He did have rales in the chest, but they were not sufficiently striking to lead the Service to take an x-ray film of the chest; therefore, I assume that the rales did not indicate a serious lung infection. I think the history would have been entirely different if the disease had started with a lung infection; he would have been sick for some time before he developed a metastatic brain abscess.

Could the source of infection have been a kidney or the tissue around a kidney? There was nothing in the record to indicate urinary symptoms. He did not complain of pain in the costovertebral region. With an acute prostatitis, which is another possibility, one would expect fever and prostration long before stupor developed. He may have had some trivial infection such as an infection of the sinus or the root of a tooth, an insignificant furuncle that had healed before the patient came into the hospital or a paronychia that was overlooked.

The final possibility is that this patient had, as a source of a metastatic brain abscess, an acute bacterial endocarditis. Such infections usually run a very acute course. I might assume that such an infection began either a week before admission, when pain in the head first developed, or as far back as three months before entry, when he first had the weakness of the right hand and when he may have had small septic infarcts from emboli to the left cerebral hemisphere. The course seems rather long to me, and no really good evidence for a bacterial endocarditis — no embolic phenomena except the petechiae — was present. I think he had staphylococcal septicemia, and a brain abscess with the origin of the infection unknown; although I am not quite willing to make the diagnosis, he may have had acute bacterial endocarditis.

DR. ALFRED KRANES: The interesting feature about this patient, whom I saw the morning after admission, was the skin lesions. The picture was otherwise quite characteristic of a patient with a cerebrovascular accident. But the rash was extraordinary; I never saw anything like it before, and it was not adequately described in the protocol. Some of the lesions were red, but the majority were almost black. They were arranged in a curious linear fashion; there was a string of them, like a series of insect bites, on the arm and across the shoulders. When I first saw them, I thought they were factitious, the result of scratching, but no scratch marks were found. In other areas there were isolated spots without the linear arrangement. On the second morning they were even more striking. About half these lesions had tiny white centers about the size of a pin point; the rest were homogeneous. On the basis of the white-centered petechiae and the cerebral accident, I thought the most likely diagnosis was a bacterial endocarditis, and so a series of blood cultures were taken, none of which showed any growth except the last two. We started the patient on huge doses of penicillin, empirically.

CLINICAL DIAGNOSES

Cerebral thrombosis, right middle cerebral artery, acute; left middle cerebral artery, old.
Hypertensive and arteriosclerotic heart disease.
Thrombocytopenic purpura.
Benign prostatic hypertrophy.
Diabetes mellitus.
?Subacute bacterial endocarditis.
?Myocardial infarction.

DR. HARWOOD'S DIAGNOSES

Staphylococcal septicemia.
Brain abscess.
?Acute bacterial endocarditis.

Anatomical Diagnoses

Bacterial endocarditis, healing, aortic valve.
Emboli and infarcts of myocardium, spleen, liver, kidneys and (?brain).
Terminal endocarditis, aortic valve.
Cardiac hypertrophy, hypertensive type.
Adenocarcinoma of prostate.

Pathological Discussion

Dr. Scully: At post-mortem examination the most interesting findings were in the heart. The aortic valve showed, along the line of closure, a row of friable brownish-red vegetations that measured up to 5 mm. in height. There were in addition small foci of calcification within the substance of the valve to which we paid relatively little attention at the time. We were surprised to find on the microscopical sections that the friable vegetations were nothing more than so-called marantic thrombi. These were composed largely of platelets; the underlying valve substance was free of inflammatory cells but showed a characteristic palisading of mesenchymal cells perpendicular to the surface. On the other hand, the calcified nodules that we had neglected grossly appeared microscopically consistent with large calcified masses of bacteria; these were surrounded by scar tissue showing chronic inflammatory-cell infiltration. The latter type of process has been described in bacterial endocarditis treated by penicillin.* It is not difficult to conceive of how the calcification of the bacterial colonies as well as their fibrous enclosure may sterilize the blood stream in such cases. Here, then, we have essentially a combination of a healing or healed bacterial endocarditis and superimposed "marantic thrombosis."

There were embolic manifestations in various organs accompanied by multiple infarcts. There was a myocardial infarction involving the posterior and lateral wall of the left ventricle that appeared to be of approximately two weeks' duration. There were also emboli and infarcts in the kidneys, spleen and liver. Unfortunately, we were not permitted to examine the brain, but I think we can safely assume that the cerebral manifestations were also on an embolic basis.

Another finding of interest was an extensive replacement of the prostate gland by adenocarcinoma. The carcinoma had also widely infiltrated the bladder wall and metastasized to a perivesical lymph node. There was also some pulmonary congestion and edema and very early bronchopneumonia.

Dr. Warren Point: Was there rheumatic endocarditis?

Dr. Scully: There was no definite evidence of rheumatic endocarditis. The fibrosis and calcification in the aortic valve could be accounted for entirely by the healing bacterial endocarditis.

Dr. Kranes: He must have healed himself, then, because he received the penicillin for only a few days before his death.

Dr. Scully: I am sure some of the healing must have taken place before he came into the hospital.

Dr. John T. Quinby: Was the heart enlarged?

Dr. Scully: It weighed 440 gm. and showed a typical hypertensive configuration. It is hard to see how *Staph. aureus* could have been the causative organism in this case because all the infarcts were bland; with *Staph. aureus*, one would expect septic infarcts.

*Moore, R. A. Cellular mechanism of recovery after treatment with penicillin: subacute bacterial endocarditis. *J. Lab. & Clin. Med.* **31**:1279-1293, 1946.

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CLINICAL ACCOUNTANCY

A. BRADFORD HILL, professor of medical statistics at the London School of Hygiene and Tropical Medicine, stands today as Britain's foremost statistician. He is, moreover, one who has been able to remove the science of statistics from its classically dust-laden atmosphere and suffuse it with a tint of life that makes its contemplation a sober satisfaction to the least mathematical-minded of clinicians. His discourse on the clinical trial, published elsewhere in this issue, is commended to all the *Journal's* readers.

Statistics in medical science has made its most luxuriant growth in that disputed land of public health, still viewed askance by so many forthright healers of the sick. In this realm — and this is perhaps the factor that renders public health still suspect — numbers rather than individuals are concerned. Statisticians and clinicians have had little in common — as has been evidenced, it may be feared, from the somewhat naïve use of statistics that has appeared from time to time in published clinical papers — even in this journal. The mutual distrust between the man of figures and the independent follower of Aesculapius was summed up two years ago in the *British Medical Journal* and is now quoted by Professor Hill: "The medical man charged with responsibility for the patient was contemptuous of the statistician's fundamental approach through the group; and the statistician took a jaundiced view of the conclusions lightheartedly drawn by the practitioner from a handful of cases without allowance for the play of chance."

Here, really, is the nub of all statistics — the foundation on which every statistical formula is based — "allowance for the play of chance." So also in the selection of material apparently at random, one must watch for the joker in the pack. Professor Hill indicated this risk in a previous publication, where mention was made of the errors that might ensue from the selection of names by the initial letter for a nutritional study (with no reference to alphabet soup). In this hypothetical study the M's and the O's were chosen at random, the unforeseen result being that the M's weighted the study with Scottish Macs, and the O's brought in a preponderance of those whose dietary habits had been formed beyond the Irish Sea.

It is necessary, to bring the minds together, for statisticians to remember that the clinician's first duty is to his patient regardless of the exact requirements of scientific analysis, and for clinicians to realize that right things must be counted if the arithmetic of the proposed study is to make any sense. Nor is it necessary to count large numbers of observations if small numbers are of equal or greater importance. As Professor Hill points out, the recovery of one case of acute leukemia after a new form of treatment has been instituted carries a weight that would require the immediate recovery of a very large number of cases of a self-limited dis-

ease to balance. Certain clinical impressions, as of the death of a patient, are indisputable: "Stone-dead has no fellow, and pre-eminent, therefore, stands the number of patients who die."

The paper carries a twofold lesson; that the medical profession has three responsibilities — to cure the sick, to prevent disease and to advance knowledge — and that in the advancement of knowledge and its accountancy, the statistician and the clinician must act as partners from the beginning of the study. The statistician, in fairness to him as well as to the success of the investigation, should have a hand in selecting the material to be counted and should not simply be called in as an accountant to audit the books after the figures have already been inked in by an amateur bookkeeper.

ROENTGENOGRAPHIC STUDIES OF THE INTERVERTEBRAL DISK

Since Mixter and Barr's disclosure in 1934 of the syndrome of ruptured intervertebral disk as a cause of pain in the lower back and "sciatica," many methods have been devised to visualize the lesion by roentgenograms. The procedure most commonly used is myelography, accomplished by injection of a contrast medium such as air, a substance dissolved in oil or a preparation that is water soluble. The last, introduced by Arnell[1] as early as 1931 but not put into common use until 1944, had considerable value over Pantopaque in that the contrast substance gives a good filling of the root sheaths and is spontaneously absorbable. It has been chiefly advocated in recent years by Lindblom,[2-4] of Stockholm, who has developed a satisfactory technic showing root compression or deformity of the dural sac. In cases of short root sheaths the contrast medium may not reach a position to show a lateral prolapse in the spinal canal. If, in addition, the distance between the disk and the dural sac is large, which often happens at the level of the lumbosacral disk, even a large protrusion may be invisible. When the extension takes place outside the spinal canal, causing compression outside the intervertebral foramens, it can never be demonstrated by myelography. To overcome these defects Lindblom devised the supplementary diagnostic method of disk puncture, for use in the lumbar region, now known as diskography.

The first studies of Lindblom, carried out in 1941 and 1944, were anatomic. Red lead was injected into the central cavities of the nucleus pulposus. When radial ruptures occurred in the annulus fibrosus, the lead passed along them to the surface of the disk. At first it was believed that puncture of the disk in living human patients might actually cause a rupture, but as this remained unproved, Lindblom proceeded to develop the method as a diagnostic test.

Disk puncture is an elaborate procedure, requiring full fluoroscopic control and a high degree of skill on the part of the operator. The direction of the needle must be extremely accurate to reach the center of the disk. The normal disk, "collar button" in shape, is filled by 0.5 cc. of contrast medium; ruptured disks will require larger quantities for good visualization. On injection of a ruptured disk, pain identical with that originally complained of by the patient may be reproduced. In a pathological specimen from one layer or both of the "collar button," a projection of dye into the annulus or through the annulus to the outside of the disk may be seen.

The method is being used with caution in a few clinics outside Stockholm. Modification of the technic by Erlacher,[5] of Vienna, appears to be an important advance. By use of a lateral puncture entrance into the subarachnoid space is avoided, and no opaque fluid finds its way into the dural sac, one of the hazards of the original procedure thus being removed. But other undesirable features have to be considered. Gardner and his associates,[6] using Diodrast as the contrast medium, found septic necrosis in 1 case out of 89 injected patients.

Lindblom has not found secondary destruction or rupture of disks after puncture, an objection raised by some investigators, but he warns that disk puncture is not an innocuous procedure that should be performed in every case of lower-back and sciatic pain. As a preoperative localization method it gives, when properly performed, better information in some cases than myelography does. The difficulty of the technic, except in large medical centers, precludes diskography as a routine measure.

The indications for its use are not entirely clear, and the dangers from faulty application are still not fully evaluated. The procedure warrants further study before being accepted as a standard diagnostic aid. Diskography may prove, as expressed by Perey,[7] to be an extremely valuable, complementary examination to myelography.

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HOME-TOWN PEOPLE

America, according to the statistical experts of the Metropolitan Life Insurance Company, despite the teeming metropolises of which it is so justly proud, is still a land of those simple people who "live and love in their home towns."

These experts, having conned the trends shown by the Census of 1950, find that three fifths of the American people still live in places with fewer than 25,000 inhabitants and that less than a fourth of them live in cities of more than a quarter million. As a matter of record 25 states have still no cities of this size, and 13 have no cities with populations of more than 100,000.

There has nevertheless been a trend, over the last half century in particular, for country people to move into the cities. Fifty years ago three fourths instead of three fifths of the population lived in communities of less than 25,000 — indeed, 11 states had no cities greater than this.

The modern tendency is for the development of suburban areas where many people may enjoy small-town life in the shadow of the cities whose advantages they also enjoy. The continuance of this trend must depend on the development of adequate and economical transportation systems; otherwise the very advantages that are sought will be choked off by growing traffic congestion.

The public health was good at San Juan, at the last advices. — It is sickly at Navy Bay and Gorgona. — Cholera has appeared at so many points, south and west, that it is quite useless to attempt keeping pace with its extension.

Boston M. & S. J. *July 28, 1852*

MASSACHUSETTS MEDICAL SOCIETY

DEATH

Smith — Fannie G. Smith, M.D., of Malden, died on July 1. She was in her sixty-second year.

Dr. Smith received her degree from Woman's Medical College of Pennsylvania in 1924. She was a former member of the Massachusetts Medical Society.

She is survived by a son.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JUNE, 1952

Résumé

Diseases	June 1952	June 1951	Seven-Year Median
Chancroid	5	4	1
Chicken pox	1275	1326	1512
Diphtheria	2	12	21
Dog bite	1772	1667	1537
Dysentery, bacillary	2	2	2
German measles	3031	422	422
Gonorrhea	155	170	310
Granuloma inguinale	0	0	0
Lymphogranuloma venereum	1	1	1
Malaria	23	12	8
Measles	2963	2556	3556
Meningitis, meningococcal	10	6	4
Meningitis, Pfeiffer bacillus	4	4	7
Meningitis, pneumococcal	2	1	4
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	0	1
Meningitis, undetermined	4	2	4
Mumps	572	1403	1004
Poliomyelitis	5	6	3
Salmonellosis	18	9	8
Scarlet fever	247	292	423
Syphilis	152	176	227
Tuberculosis, pulmonary	155	188	192
Tuberculosis, other forms	11	12	13
Typhoid fever	0	2	2
Undulant fever	1	1	2
Whooping cough	98	93	500

Comment

Diseases below the seven-year median were chicken pox, diphtheria, mumps, scarlet fever and whooping cough.

The 2 cases of diphtheria and the 247 cases of scarlet fever represented the lowest number ever reported for either disease for this month since 1906.

The 98 cases of whooping cough represented the next to the lowest number of cases reported for this month since 1915, the lowest being June, 1951, when 93 cases were reported.

The 572 cases of mumps was the lowest number ever reported for June since 1946, and next to the lowest since 1939.

Diseases above the seven-year median were German measles and measles.

The 3031 cases of German measles reported for June was the highest since 1943. However, this represented a drop from the preceding month of May, when 3918 cases were reported (the highest number of cases for 1952).

Although 2963 cases of measles were reported for June, this represented the lowest number of cases for the year so far and a marked drop from the preceding month of May, when 5845 cases were reported. Measles can now be considered definitely on the decline after having apparently reached a peak in February, when 12,991 cases were reported.

Geographical Distribution of Certain Diseases

Diphtheria was reported from: Lynn, 1; Peabody, 1; total, 2.

Dysentery, amebic, was reported from: Springfield, 1.

Dysentery, bacillary was reported from: Fitchburg, 1; Westboro, 1; total, 2.

Encephalitis, infectious, was reported from: Malden, 1; Norwood, 1; Quincy, 1; total, 3.

Hepatitis, infectious, was reported from: Auburn, 2; Boston, 1; Bourne, 1; Camp Edwards, 1; Newton, 1; Worcester, 3; Wrentham, 4; total, 13.

Leprosy was reported from Chicopee, 1.

Malaria was reported from: Camp Edwards, 6; East Longmeadow, 1; Fort Devens, 13; Haverhill, 1; Lawrence, 1; Peabody, 1; total, 23.

Meningitis, meningococcal was reported from: Boston, 5; Brockton, 1; Dalton, 1; Fall River, 1; Haverhill, 1; Malden, 1; total, 10.

Meningitis, Pfeiffer bacillus, was reported from: Nantucket, 1; Quincy, 1; South Hadley, 1; Worcester, 1; total, 4.

Meningitis, pneumococcal, was reported from: Boston, 1; Worcester, 1; total, 2.

Meningitis, mumps, was reported from: Marblehead, 1.

Meningitis, undetermined was reported from: Boston, 1; Clinton, 1; Quincy, 2; total, 4.

Poliomyelitis was reported from: Hinsdale, 1; Lynn, 1; Quincy, 1; Springfield, 1; Worcester, 1; total, 5.

Rocky Mountain spotted fever was reported from: Palmer, 1.

Salmonellosis was reported from: Belchertown, 1; Boston, 3; Cambridge, 2; Everett, 2; Lawrence, 1; Melrose, 1; Salem, 1; Springfield, 2; Westboro, 4; Worcester, 1; total, 18.

Septic sore throat was reported from: Boston, 1; Cambridge, 2; Fall River, 2; Lynn, 1; Warren, 1; Worcester, 1; total, 8.

Tetanus was reported from Lawrence, 1.

Trichinosis was reported from Boston, 1; New Bedford, 1; total, 2.

Tularemia was reported from: Falmouth, 1.

Undulant fever was reported from: Medfield, 1.

CORRESPONDENCE

REGARDING A STATE MEDICAL SCHOOL

To the Editor: As the only physician on the Recess Commission on University of Massachusetts Medical and Dental Schools, I should like to answer your editorial of June 12 attacking the establishment of a state medical school.

It seemed to the Commission that the question of the need of a new medical-dental school resolves itself into two parts:

(1) Is there a real need for more practicing physicians in Massachusetts now or in the near future?

(2) Are there enough qualified young people interested in studying medicine? A corollary of this is, Do adequate facilities now exist for their training in Massachusetts and in schools outside the State?

The question of establishment of a medical school by a university other than the state university can be dismissed quickly since private medical schools have constituted a drain on university budgets, and it is therefore unlikely that a new school would be built by a university other than a state university. Of the 12 new schools now contemplated, only 1 (Yeshiva) is a privately endowed school. Also readily dismissed is the proposal that the State should help already existing medical schools to expand: this is unconstitutional — Massachusetts cannot help private educational institutions.

Supply of Physicians

In Massachusetts there are 8688 physicians according to the A.M.A. *Directory*. How many of these physicians are actively engaged in practice cannot be determined since Massachusetts is one of only 14 states not requiring periodic registration. The ratio of physician to population here is 1:538, one of the highest in the United States. But such a basis for determining need is very unsound, as is average income of physicians, since distortion of both figures occurs in teaching centers because of large numbers of young physicians training in these states. Such persons add to the numbers and decrease the average physician income. (New York State has the highest ratio of doctors to population and one of the lower average physician incomes but still took over two medical schools recently.)

Of greater importance is the situation as regards general practitioners. Of the 3042 physicians in Massachusetts classified as general practitioners, almost half (48 per cent) are graduates of unapproved schools! Since these schools are now closed, there will be a dwindling supply of general practitioners. Already 43 per cent of licensed practitioners in Massachusetts come from outside the State. It is unlikely that this number would be increased to compensate for the output of closed schools. A state medical school would help meet this demand. Since applicants would be largely restricted to Massachusetts residents, they would tend to remain in their home state, according to Dr. Weiskotten, chairman of the Council of Medical Education of the American Medical Association. In effect, the new school would be graduating well equipped physicians to replace the large number of graduates of unapproved schools. It is interesting that the need of more physicians is more apparent to those physicians engaged in active practice than it is to those in the rear echelons.

According to Dr. Weiskotten, the optimal size of a medical-school class is 100. Harvard and Tufts already have over 100 per class. Boston University, with 72, is the only one capable of expansion. As to the effect upon existing schools of the establishment of a new school the following remarks are of interest. They were written, not in 1952, but in 1867!

> While we are in no danger of having too many academic schools and scholars, the unnecessary multiplication of medical students, by the efforts of more institutions competing with each other to fill their classes is an injury to the profession and community. . . It is very difficult to obtain instructors fully skilled in the profession . . . competition between Medical Schools has tended to decrease the character and quality of their education . . . multiplication of schools divides emoluments and deteriorates instruction.

These statements were made in 1867 by the medical leaders opposing the establishment of Tufts College Medical School (*History of Tufts College Medical School, 1893-1943*. By Benjamin Spector, M.D.).

The demand for physicians at the intern level can be appreciated from the results of the Matching Plan: there were 10,414 approved internships in the United States for 5681 applicants.

Qualified Applicants

In 1950–51 there were 22,279 applicants for 7182 freshman openings in medical schools (a ratio of 3:1). In 1927–28 there were 11,289 applicants for 6199 openings, or a ratio of about 2:1. It is, of course, true that many of the applicants are not qualified to study medicine. Yet there should be an adequate number of qualified Massachusetts applicants who have oriented their college training toward medical school to fill a new medical school of 100 per class. Only 41 per cent of the enrollment of the Massachusetts medical schools now comes from Massachusetts. Of the 227 Massachusetts medical-school freshmen in the United States, 138 are in Massachusetts schools and 89 in schools of other states. Schools outside Massachusetts are restricting applicants more and more to their own state or area. Seventeen of the seventy-two four-year medical schools now limit enrollments to residents of their own state and twelve more limit entrants to their own region, 43 schools admitting both residents and nonresidents have limited the number of nonresidents.

In the country as a whole there were 25,633 students enrolled in 1950, whereas there were 26,147 enrolled in 1905. To be sure, the training of many of these students in 1905 left much to be desired, but they became practicing physicians for better or worse and would be counted in a physician census.

The Commission came to the following conclusion:

(1) There is a real and growing need for physicians, particularly general practitioners, in Massachusetts.

(2) There is an adequate number of qualified Massachusetts applicants. Further restrictions by out-of-state schools will further reduce their opportunities to study medicine.

(3) Present schools, except for Boston University, cannot expand without impairing the quality of instruction.

(4) A new medical school can be built only by the State; no other universities are contemplating new medical schools.

(5) Such a new school should have top quality administration and faculty, this being far more important than the physical plant.

The proposed graduate school offered as a substitute in your editorial is so ill conceived and impractical that it is hard to believe that it appears on the editorial page of the official organ of the Massachusetts Medical Society. How can such a plan increase the number of doctors in Massachusetts? Doesn't the writer know that such aid is unconstitutional? If such a program were properly conducted, would not the expense be far greater than the annual budget of a medical school? Would you not increase the percentage of specialists? Would you not be training more physicians at public expense to return to their homes outside the State? Who would administer this project? It would be far better to help men in general practice, particularly graduates of unapproved schools, to keep up with newer advances (the Gallupe Plan sponsored by the Massachusetts Medical Society has been rendered only lip service.)

Finally, it should be pointed out that, to the best of my knowledge, no medical school has ever been sponsored or endorsed by a medical society (except for New Jersey). It is to be hoped that if a new Massachusetts Medical and Dental School is established, it will receive the blessings and cooperation of the medical and dental groups.

DAVID HURWITZ, M.D.

Cambridge, Massachusetts

Note: The editorial in question made no "attack" on any persons, things or ideas. It suggested that "one might question how far the establishment of a fourth school in Boston would contribute to the number of physicians settling in Massachusetts."

The proposal that Dr. Hurwitz finds "so ill conceived and impractical that it is hard to believe that it appears on the editorial page of the official organ of the Massachusetts Medical Society" was merely a suggestion "that consideration be given to the establishment of a new and different type of graduate school of medicine in the State."

The editors plead guilty to ignorance of the relative constitutionality of establishing one type of medical school instead of another. — ED.

PROBLEMS OF NOMENCLATURE

To the Editor: I fully appreciate that arguments about nomenclature are often fruitless. However, I think it is important for such a journal as the *New England Journal of Medicine* to use proper terminology as frequently as possible.

I was disappointed to see the term "malignant hypertension" used in one of the editorials, entitled "New Therapeutic Hazards, in the June 12 issue. *The Standard Nomenclature of Diseases and Operations*, 4th edition, 1952, published by the American Medical Association, classifies hypertension as: hypertensive vascular disease or essential vascular disease. I much prefer the first definition, since there is nothing essential about "essential" vascular disease as implied in the second.

It seems most important to be as accurate as possible in describing a disease about whose etiology and natural course so little is known. If one wished to describe a rapidly progressive phase as occurs at times in hypertensive vascular disease the term "accelerated phase" or "advanced" would be descriptive. Such terms as "benign" and "malignant" are very ambiguous, and their use should be discouraged especially in the *New England Journal of Medicine*.

The term "malignant" nephrosclerosis is equally poor to my way of thinking, even though it is included in the *Standard Nomenclature*. Perhaps Dr. Castleman would consider a more descriptive term such as "necrotizing" nephrosclerosis or advanced nephrosclerosis as preferable to "malignant" nephrosclerosis in diagnosing such a case as one of the recent Cabot cases. It seems wise to be consistent and to use descriptive terms in describing the anatomic as well as the clinical findings.

Boston, Massachusetts JAMES H. CURRENS, M.D.

UNION HEALTH DEPARTMENTS

To the Editor: The Board of Health of Milton wishes to go on record as definitely opposed to the mandatory provisions of the act relative to the organization of union health departments. We concede that the Massachusetts Department of Public Health is within its rights in informing boards of health what functions it considers a board should provide, but it has no right to dictate to a board *what* it should do and more specifically *how* it should do it.

There are four main sections of the Minimum Health Service Requirements of the Department of Public Health and the Public Health Councils to which we take specific exception. These are as follows:

"Set up and maintain, or otherwise provide, a public Health Laboratory Service. . . ."

We maintain that the State already provides this service, to which each town contributes by taxation, that if a town wishes to use it, it may do so, and that the setting up of a laboratory is duplication of expenses.

Personnel — "A full-time director of Health. . . a full-time supervising sanitary officer. . .one sanitarian for every 25,000 population. . .one full-time chief clerk. . .one full-time stenographer per 15,000 population."

We believe this staff to be not only unnecessary but actually ridiculous. Two sanitary engineers in a community of 35,000 persons would find it impossible to keep occupied. The staff of clerks would die of ennui. By implication even the Department admits that a full-time director is unnecessary, since it would permit one full-time officer to service several towns under the Union Health Department, which means that each town could have only part-time service from him!

Budget — The $1.00 per capita has been increased to $1.50, which means that a town (taking Milton as an example) that in our opinion provides adequate services for $10,000 must spend $35,000. We do not believe that the taxpayers will receive any improved services merely by spending this extra amount.

Under Section V of the act itself — "All persons holding office or employment. . . in the Union Board of Health. . . shall be subject to Chapter III, of the General Laws. . . and the positions placed within the civil service."

To require a town to accept the civil-service law is entirely divorced from public health. The law is permissive, and this would make it mandatory.

One of the Presidential candidates in his opening campaign speech took cognizance of this whole matter, as follows:

Another evil which threatens us is the gradual absorption by the central government of functions that belong to local communities and to individuals. The stifling and costly bureaus that spring out of this process are manned by experts in self-perpetuation and ceaseless expansion. . . government must be so organized that we feel confident we haven't lost sight of such things as thrift, frugality, and economy. . .needed. . .is the efficient limitation of government functions and the curbing of their spread into new and overlapping fields.

Paul R. Withington, M.D.
James L. Coombs
Paul V. McPeake

Milton, Massachusetts

NONCLINICAL NOTES

SHATTUCK PROFESSOR

Dr. Arthur T. Hertig, pathologist and senior obstetrician of the Boston Lying-in Hospital and pathologist of the Free Hospital for Women, has been appointed Shattuck Professor of Pathological Anatomy at the Harvard Medical School, to succeed Dr. S. Burt Wolbach, who retired in 1947.

Dr. Hertig, a native of Minnesota, graduated from the University of Minnesota in 1928 and from Harvard Medical School in 1930.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Relation of Psychological Tests to Psychiatry. Edited by Paul H. Hoch, M.D., New York State Psychiatric Institute and Columbia University College of Physicians and Surgeons, and Joseph Zubin, Ph.D., New York State Psychiatric Institute and Department of Psychology, Columbia University. 8°, cloth, 301 pp. New York: Grune and Stratton, 1952. $5.50. The proceedings of the fortieth annual meeting of the American Psychopathological Association, held in New York City in June, 1950.

The 1950 meeting of the American Psychopathological Association was devoted to a symposium on psychologic tests and their relation to psychiatry. A number of well known specialists read and discussed papers on various aspects of the subject. The material is divided into five parts: historical bases, diagnostic use, the influence of exogenous factors, the influence of the psyche on psychologic test performance and the presidential address. There is a good index and the book is well published.

Dynamic Psychiatry: Basic Principles. Volume I. By Louis S. London, M.D. 8°, cloth, 98 pp. New York: Corinthian Publications, Incorporated, 1952. $2.00.

In this small book Dr. London writes on the evolution of psychotherapeutics from antiquity to the time of Freud; he discusses the meaning of the dream and the psychology and development of the libido in the child and in the adult. The interesting short preface describes the relations of Freud with his famous pupils, Adler, Jung and Stekel. The book is well indexed and well printed.

Heredity in Uterine Cancer. By Douglas P. Murphy, M.D., assistant professor of obstetrics and gynecology and research associate, Gynecean Hospital, Institute of Gynecologic Research, University of Pennsylvania. 8°, cloth, 128 pp., with 51 tables. Cambridge, Massachusetts: Published for the Commonwealth Fund by the Harvard University Press, 1952. $2.50.

Dr. Murphy reports on his study of the familial occurrence of cancer of the uterus, conducted among the relatives of 201 women afflicted with the disease and checked with the findings in 215 control families. A total of 6445 persons were studied. The results of the survey are summarized briefly: The evidence supports the conclusion that hereditary factors affect the frequency with which cancer appears in the uterus; factors that predispose to uterine cancer do not predispose in any significant degree to cancer in other sites; hereditary factors, other than those concerned with uterine cancer, play a role in the etiology of cancer elsewhere in the body. The monograph is well published.

Disorders of the Heart and Circulation. Edited by Robert L. Levy, M.D., professor of clinical medicine, Columbia University College of Physicians and Surgeons, and attending physician, Presbyterian Hospital, New York. 8°, cloth, 944 pp., with illustrations. New York: Thomas Nelson and Sons, 1951. $12.00.

Dr. Levy has compiled in this volume the 34 articles written for *Nelson's Loose-Leaf Medicine* during the past three years by over 40 contributors, specialists in cardiology. Various aspects of diseases of the heart and arteries are discussed. Boston is well represented by 9 physicians, including Merrill C. Sosman, Howard B. Sprague, Conrad Wesselhoeft and Paul D. White. There is a good index and the book is well published. The opportunity is provided for obtaining this special collection of articles on the heart and related subjects without the necessity of purchasing the loose-leaf set. The book should be in all medical libraries and in the collections of cardiologists.

Pathology of the Fetus and the Newborn. By Edith L. Potter, M.D., Ph.D., associate professor of pathology, Department of Obstetrics and Gynecology, University of Chicago, pathologist, Chicago Lying-in Hospital, and chief pathologist, Chicago Department of Health. 4°, cloth, 574 pp., with 601 illustrations. Chicago, Illinois: The Year Book Publishers, Incorporated, 1952. $19.00.

Dr. Potter has based her book on eighteen years' experience with the fetus and the newborn infant. The subject is thoroughly covered and lists of references are appended to the various chapters. There is a very good index, and the illustrations are excellent. The printing is well done, with a good type. The book should be in all medical libraries and available to obstetricians and pediatricians.

Modern Electrocardiography. Volume I: The P–Q–R–S–T–U Complex. By Eugene Lepeschkin, M.D., assistant professor of experimental medicine, University of Vermont College of Medicine. With a foreword by Frank N. Wilson, M.D., professor of medicine, University of Michigan Medical School. 4°, cloth, 598 pp., with 91 illustrations. Baltimore: The Williams and Wilkins Company, 1951. $12.00.

Dr. Lepeschkin has set himself the task of presenting a comprehensive but concise summary of the progress of electrocardiography since 1933, when the multiple precordial leads were first introduced by Dr. F. N. Wilson and his school. The present volume discusses the form of the electrocardiogram in the regularly beating heart. Volume II will be devoted to disturbances of the cardiac rhythm. The text is devoted to the fundamentals of the subject and the influence of various conditions on the cardiogram. A bibliography of 9999 references is appended to the text, and there is a good subject index. The printing is well done, with a good, large type. The book should be in all medical libraries and in all collections on the subject.

Adrenal Cortex: Transactions of the Second Conference, November 16–17, 1950, New York. Edited by Elaine P. Ralli, M.D., Department of Medicine, New York University College of Medicine. 8°, cloth, 209 pp., with 68 illustrations and 14 tables. New York: Josiah Macy, Jr., Foundation, 1951. $3.00.

Complete sets of these conference reports should be in all medical reference collections.

A Textbook of Clinical Neurology: With an introduction to the history of neurology. By Israel S. Wechsler, M.D., clinical professor of neurology, Columbia University, and consulting neurologist, Mount Sinai, Montefiore and Rockland State Hospitals, New York. Seventh edition. 8°, cloth, 801 pp., with 179 illustrations. Philadelphia: W. B. Saunders Company, 1952. $9.50.

This well known authoritative textbook was first published in 1927. This new edition has been revised to bring the material up to date. Much of the text has been rewritten and new material has been added on electromyography and double simultaneous stimulation. The lists of references have been revised; there is a good index, and the publishing is excellent. The book is recommended for all medical libraries and to all physicians interested in neurology.

Clinical Practice in Infectious Diseases for Students, Practitioners and Medical Officers. By E. H. R. Harries, M.D. (Lond.), F.R.C.P., and M. Mitman, M.D. (Lond.), F.R.C.P., consultant physician and medical superintendent, River Hospitals, Joyce Green, Dartford. With the collaboration of Ian Taylor, M.D. (Lond.), M.R.C.P., senior medical officer (infectious diseases), Public Health Department, London County Council. Fourth edition. 4°, cloth, 717 pp., with 48 illustrations and 27 tables. Baltimore: The Williams and Wilkins Company, 1951. $6.50.

This standard British book was first printed in 1940 and has been out of print for over a year. The first edition was translated into Spanish. There has been some rearrangement of the text, and more illustrations in color and halftone have been added. Lists of selected references have been added to the various chapters, and there is a good index. The printing was done in Great Britain.

Standard Nomenclature of Diseases and Operations. Richard J. Plunkett, M.D., editor, and Adaline C. Hayden, R. R. L., associate editor. Fourth edition, 8°, cloth, 1034 pp. New York: Published for the American Medical Association by the Blakiston Company, 1952. $8.00.

The last edition of this standard nomenclature was published in 1942. The text has been thoroughly revised by a group of specialists. Approximately 5800 changes have been made, exclusive of the necessary revisions of the international list. There is a comprehensive disease index and one of operations. The book is well published and should be in all medical libraries.

Die gesunde und kranke Wirbelsäule in Röntgenbild und Klinik: Pathologischanatomische Untersuchungen. Von Geh. Med. Rat. Prof. Dr. med. et Dr. med. vet. h.c. George Schmorl. Für Röntgenkunde und Klinik bearbeitet von Prof. Dr. med. habil. Herbert Junghanns, Oldenburg (oldb.). Second edition. 4°, cloth, 284 pp., with 399 illustrations. Stuttgart: Georg Thieme, 1951. Ganzleinen DM 69.– Distributed by Grune & Stratton, Inc., New York.

The first edition of this well known special book was first published by the late Dr. Schmorl in 1932. Dr. Junghanns has thoroughly revised the text to bring it up to date. There is an extensive bibliography. The illustrations and printing are excellent. The lack of an index detracts from the reference value of the book. It is recommended for all collections on the spine in health and disease.

A Textbook of Clinical Pathology. Edited by Seward E. Miller, M.D., medical director, United States Public Health Service, and chief, Division of Occupational Service, Washington, D. C. Fourth edition. 4°, cloth, 1060 pp., with illustrations. Baltimore: The Williams & Wilkins Company, 1952. $9.00.

This book was first issued in 1938 and since then has gone through four editions and six reprintings, which speaks well for its soundness and popularity. The book is the joint effort of eight specialists and is designed to present in one volume the basic scientific information in its field. The text has been completely rearranged and rewritten. Many of the highly technical procedures have been omitted. Short bibliographies of the pertinent literature are appended to the various chapters. The publishing is well done, and the book should be in collections on the subject.

The Child in Health and Disease: A textbook for students and practitioners of medicine. By Clifford G. Grulee, M.D., Rush Professor of Pediatrics, University of Illinois, attending pediatrician, Presbyterian Hospital, Chicago, and chief editor, *American Journal of Diseases of Children*, and R. Cannon Eley, M.D., assistant clinical professor of pediatrics, Children's Hospital, Children's Medical Center, Harvard Medical School, and chief of Isolation Service and visiting physician, Infants' and Children's Hospitals, Boston, and member of the committee on nominations of the American Academy of Pediatrics. Second edition. 4°, cloth, 1255 pp., with illustrations. Baltimore: The Williams & Wilkins Company, 1952. $15.00.

The first edition of this composite book was published in 1948. This new edition, the work of eighty-seven specialists, has been completely revised and brought up to date. New chapters have been added on adoption, medical supervision of summer camps, cardiovascular surgery and viral hepatitis. Short lists of references are appended to the various chapters and there is a comprehensive index. The book should be in all collections on pediatrics.

Intergovernmental Relations in Public Health. By Laurence Wyatt, Yale University. 4°, paper, 212 pp. Minneapolis: The University of Minnesota Press, 1951. $3.50. (Intergovernmental Relations in the United States, Research Monograph Number 4.)

The studies made in this monograph are based on observations in the state of Minnesota. The greater part of the text is devoted to a discussion of the United States Public Health Service, the United States Children's Bureau, their interrelation and the grants-in-aid program. The remainder of the text is devoted to state and local health departments and interstate and local relations. The book should be in all collections on public health.

Kymographische Röntgendiagnostik: Zur Beurteilung [illegible] Herzens in Beispielen. By Professor Dr. Pleikart Stumpf, München. 8°, cloth, 119 pp., with 164 illustrations. Stuttgart: Georg Thieme, 1951. Kartoniert DM 25.50. Distributed by Grune & Stratton, Inc., New York.

This monograph describes the use of kymographic x-ray diagnosis of diseases of the heart and aorta. It is well illustrated and there is a good index.

NOTICES

ANNOUNCEMENT

Dr. Chester Joseph Dexter announces the opening of his office for the practice of general surgery at 51 Brattle Street, Cambridge.

MASSACHUSETTS CIVIL DEFENSE TRAINING SCHOOLS

A series of regional staff college meetings, sponsored by the Civil Defense Agency of the Commonwealth of Massachusetts, is being held on the following subjects: civil-defense law; administration and finance; research and development; and public information. In addition, a series of regional Army Ordnance schools is being conducted for the purpose of orientation and instruction of civil-defense agents in the identification, verification and reporting of explosive hazards (general ordnance, guided missiles and atomic and hydrogen weapons) and in preliminary safety meetings.

The meetings and schools are held from 10 a.m. to 3 p.m. The schedules of dates and places may be obtained from the director of the Civil Defense Agency, 334 Boylston Street, Boston.

PHYSICAL THERAPISTS FOR CARE OF PATIENTS WITH POLIOMYELITIS

Physicians may obtain information regarding qualified physical therapists available for patients in the convalescent stage of poliomyelitis from the following members of the American Physical Therapy Association: Connecticut, Mrs. Lenora Grissell; Rhode Island, Helen Babcock; Maine, Miss Lois Burns; Vermont, Miss Lillian Kron; New Hampshire, Miss Mary Bullock; Massachusetts, Mrs. Nina Nichols; Worcester Area, Mrs. Mary T. Hynes; and Springfield Area, Mrs. Ruth S. Whitman.

GRANTS IN CANCER RESEARCH

The Committee on Growth of the National Research Council, acting for the American Cancer Society, is accepting applications for grants in support of cancer research. Applications for new grants received before October 1 will be considered during the winter, and grants recommended at that time will become effective July 1, 1953. Investigators now receiving support will be notified individually regarding application for renewal of these grants.

The Committee believes that a clear understanding of cancer must rest upon a deeper insight into the nature of the growth process, normal and malignant. Therefore, the scope of the research program is very broad and includes, in addition to clinical investigations on cancer, fundamental studies in the fields of cellular physiology, morphogenesis, genetics, virology, biochemistry, metabolism, nutrition, cytochemistry, physics, radiobiology, chemotherapy, endocrinology and environmental cancer.

During the past year the American Cancer Society, Incorporated, on recommendation of the Committee on Growth, has awarded approximately 250 grants totaling about $1,700,000. A program of similar magnitude is contemplated for the coming year.

Application blanks and additional information may be obtained from the Executive Secretary, Committee on Growth, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

(*Notices concluded on page xi*)